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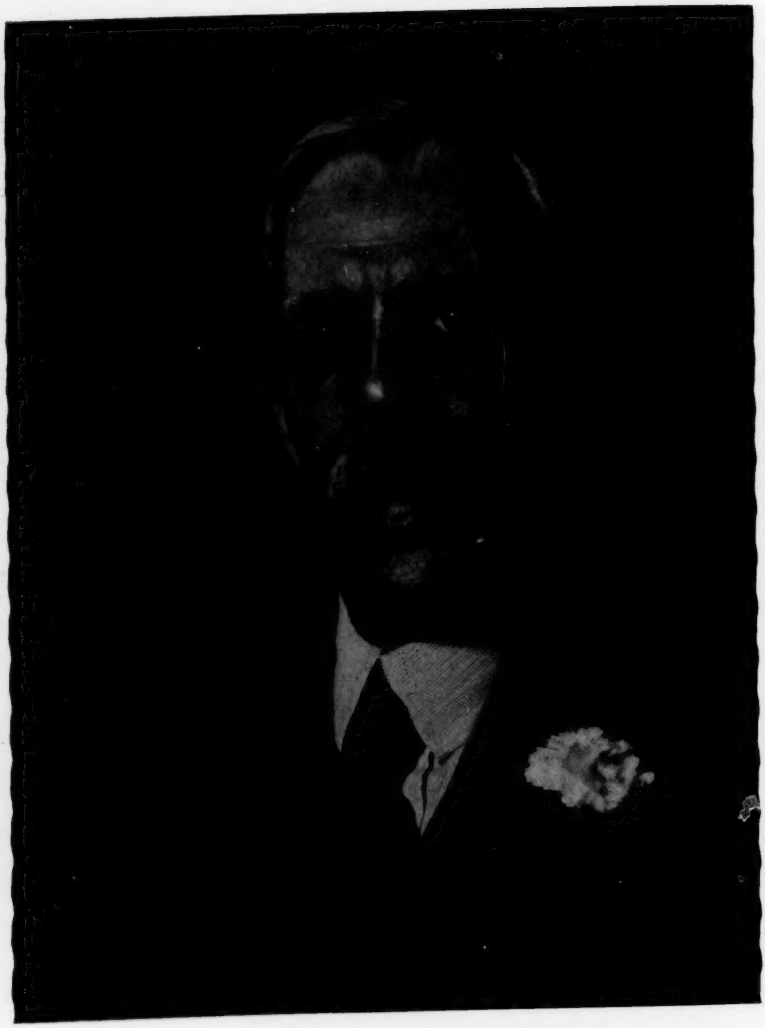

SIR JOHN HERBERT PARSONS

*C.B.E., D.Sc., LL.D., F.R.C.S., F.R.S.*

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## COMMUNICATIONS

### SIR JOHN HERBERT PARSONS

**An Appreciation**

BY

PROFESSOR E. D. ADRIAN, O.M., F.R.S.

IN this tribute to Sir John Parsons for his 80th birthday the contributors are all, with one exception, ophthalmologists or his former pupils. The exception is the writer of this introduction, who has never had the privilege of his teaching and knows next to nothing of clinical ophthalmology. Yet a physiologist may claim the right to join with pathologists and clinicians in any volume covering the whole field of Sir John's activities. His scientific studies of the problems of vision have meant so much to us and to psychologists, too, that we must not be denied the pleasure of wishing him well.

It has never been easy to combine the busy life of a consulting physician or surgeon with research into the basic problems of natural science, though fortunately exceptional people have managed to do it in the past and are doing it even now. But it must be still more difficult to remain both the recognised authority on the science and the recognised leader in the practice of a branch of medicine, to remain our foremost authority on the physiology of vision as well as the dominant figure in the British School of Ophthalmology, and in this School not only the teacher but the organiser of teaching and research, the adviser of governments, and the expert whose opinion is indispensable in all the varied problems where human vision is concerned. This is the position which Sir John Parsons has held for many years. Physiologists may grudge some of the time he has had to spend in the wards and committee rooms, and clinicians may have wished for even more of his help, but neither can deny his outstanding position in the science and practice of ophthalmology.

His early training certainly qualified him for the work he has done. The influence of Lloyd Morgan at Bristol and of Schafer at University College might have kept him to the narrower path of academic psychology or physiology. Though his wide interests and general kindliness must be innate, the years spent in general practice were surely not wasted: we can still go to him with our troubles and feel the better for his advice. And when he finally turned to ophthalmic surgery what better surroundings could he have found than those at Moorfields and at University College Hospital?

I have no right to speak of the influence which he has had in these two centres of scientific medicine, but I can speak of the influence of his writings on all physiologists who have studied the sense organs. His book on colour vision was first published in 1915 and has remained our surest guide through the intricacies of a fascinating subject. The great originator of it all, Sir Isaac Newton, did not like hypotheses and Thomas Young's three colour

theory ran very close to the facts which he discovered, but from the time of Goethe to the present day the subject has been beset with speculation and the proportion of new theories to new facts has been dangerously high. Sir John's book was a masterly analysis of the facts and an unbiassed examination of the theories, both rare delights. Much of the material was assembled for the first time and given orderly presentation and meaning. His book soon became the classical work of reference on colour vision and its redressing of the balance between fact and theory gave a new impetus to the subject. The impetus has remained and much of the present day interest in colour vision can be traced to this source.

Having reviewed the physiology of vision Sir John showed his wide knowledge of the border lands of neurology and psychology in his "Introduction to the Theory of Perception." In this, too, he brought together a wealth of information and showed its relevance to the general problem. But though these two books are the concrete expression of his work in the field of academic science they are by no means his sole contribution to it. He has achieved as much or more by his personal influence, by his constant and powerful advocacy of research on visual physiology, and by his kindly support of the young research worker. His colleagues in the Royal Society and on the Medical Research Council know him as a wise and honest councillor with the initiative needed for the planning of new developments and the experience needed for carrying them through. His pupils and friends everywhere know him as one who inspires their warm affection as well as their admiration for what he has done. We offer him our most cordial greetings and our sincere congratulations on his birthday.

## SIR JOHN HERBERT PARSONS

*An appreciation*

BY

Professor J. VAN DER HOEVE

SIR JOHN HERBERT PARSONS reaches the age of 80 years on September 3rd of this year. His whole life has been devoted to his and our beloved profession; ophthalmology in England is greatly the gainer for his work and his reputation is truly international.

His writings on all aspects of ophthalmology are numerous and well known; and in addition to his professional activities, he served his country, both in war and in public life in peace, in many capacities. For these services many honours were accorded to him. My tribute to him, however, is essentially concerned with the work he has done for the International Council of Ophthalmology, a sphere wherein we worked together and where I knew him best. After the first World War an Anglo-American Convention of Ophthalmology was held in 1925 when a Committee for reviving the International Congresses was nominated. The English members of the Committee were Treacher Collins, Sir John Parsons and Leslie Paton. As a result a meeting was held at Scheveningen in 1927, where there gathered 50 oculists from 25 different nations, and here the plans were laid for the Congress of 1929. It is interesting that we met again afterwards in the same year (1927) when we each received the degree of Ll.D. at Edinburgh.

In the name of the oculists who serve on the International Council of Ophthalmology, I wish from the very bottom of my heart that Sir John will still have many more years of good health and happiness.

# SIR JOHN HERBERT PARSONS

## An Appreciation

BY

R. R. JAMES

" *Time hath, my Lord, a wallet at his back,*
*Wherein he puts alms for oblivion ;* "

TROILUS AND CRESSIDA, ACT 3, SCENE 3.

ULYSSES, in the play, calls the wallet a "great-siz'd monster of ingratitudes."

In my case the wallet holds no ingratitudes ; but as one gets older it naturally becomes fuller and fuller. It will, however, never be so full that I can forget all I owe to Sir John Parsons. It is now more than forty-one years since I was first introduced to him at one of the evening meetings of the Ophthalmological Society by a common friend. I have never forgotten how he said, when he was informed that I was hoping to come and work with him at Moorfields, that ophthalmology was already overfull. He must have noticed the chagrin in my looks for he quickly added : " Of course there's always room for a good man."

I became his clinical assistant at the end of the year 1907 and have been intimately associated with him for more than thirty years. I bear to none of the companions on life's journey so much real, almost filial, affection as I do to Sir John Parsons. He has been a most strong Tower to British Ophthalmology and especially to the Journal, standing ever,

" Four-square to all the winds that blew."

That he may long continue to be the Doyen of our branch of the profession is the fervent desire of all who have been associated with him.

# DEVELOPMENTAL APHASIA

## Also known as Congenital Word-blindness and sometimes referred to as Alexia or Dyslexia

BY

A. H. H. SINCLAIR

EDINBURGH

THIS remarkable developmental failure is met with in various sensory-motor affections and may be manifested in functional failure in connection with sight, hearing, kinaesthetic performance and probably in other functional activities.

We are here concerned with developmental aphasia connected with vision, also referred to as congenital word-blindness. This disability is met with in children but does not become obvious until the child has been confronted with the problem of learning to read. The condition does not depend on the degree of general intelligence but is met with in all grades of natural ability, including occasionally individuals of the highest intelligence, which renders it all the more important that the nature of the disability should be clearly recognised. It does not depend on failure of vision due to errors in refraction or difficulty in focusing, or other causes found in the eye, though such should always receive treatment when present. This condition is a failure in visual comprehension, caused by delayed development of unilateral hemispherical dominance and failure in word-memory and relates to the psychology of vision: letters and words are seen but not recognised. Fortunately aural perception is available and eagerly used by children suffering from this visual embarrassment and proves to be of great value to them.

There is a natural tendency to recovery in all children so affected which increases progressively with the child's development and education. The condition may be mild and transitory or severe and difficult to overcome. The cases form a graded series, including all degrees of severity. In the milder cases recovery often takes place in the ordinary course of school education: in the more severe cases persistent skilled instruction, undertaken early, is essential. In the Edinburgh Primary Schools about 10 per cent. of the children were found to be affected by developmental aphasia, of whom half recovered in the ordinary course of school education, while the remainder required special treatment.

Teachers of children may fail to recognise the fundamental cause of the symptoms and this was appreciated by Hinshelwood in 1896 when he wrote: " It is a matter of the highest importance

to recognise the true nature of this difficulty in learning to read . . . otherwise these children may be harshly treated or punished for a defect for which they are in no wise responsible." The thwarting effect of this disability, especially in highly intelligent children in whom it often appears, gives rise to emotional disturbances which vary according to the temperament of the child and may produce inferiority complex, a defiant attitude to instruction, carelessness or inattention from hopelessness and sometimes fits of crying. The connection between such symptoms and their fundamental cause has frequently remained unrecognised by teachers, but is evident to the trained observer.

Developmental aphasia has doubtless always been present amongst schoolchildren, though unrecognised, and an outstanding example of this would seem to be provided by the early life-history of the famous surgeon, John Hunter. Up to the age of 17, Hunter showed very clearly that he was in every respect, apart from book-learning at school, a highly intelligent boy, possessed of character and a great desire to understand the facts and the mysteries of the natural objects of country life in the midst of which he grew up. It was only when he was confronted with learning to read, that is, to comprehend facts and ideas through the recognition of printed symbols, that he failed to progress. He was sent to a good school where his older brothers, James and William, had excelled, but John could not learn to read. All his biographers insist on this remarkable fact in John Hunter's early life. In addition it is recorded of him that he suffered from prolonged fits of crying after he was beyond the age when such evidence of emotional distress is met with in boys.

The failure to learn to read and write in the case of a boy of John Hunter's ardent and enthusiastic temperament and the knowledge that his brothers had succeeded so well at the same school must have caused him great disappointment and distress.

He was the youngest in a family of ten and lived in a cultivated and intellectual circle where all enjoyed the advantages of learning from books, but John Hunter was denied this source of knowledge for which he possessed such an insatiable appetite. Nobody could understand why he failed to learn to read and write, when he could and did learn so much through other channels, by actual contact with phenomena, by the observation of things and by hearing others talk or read. His own recorded words are: "When I was a boy I wanted to know about the clouds and the grasses, and why the leaves changed colour in the autumn: I watched the ants, bees, birds, tadpoles and caddis worms; I pestered people with questions about what nobody knew or cared anything about." The enthusiasm of his genius, however, impelled him into the new fields of

personal observation and study in which he later so greatly excelled.

Only in the light of knowledge which was not possessed until 150 years later could the true nature of John Hunter's disability have been recognised as an example of developmental aphasia.

But even in modern times these cases may remain unrecognised: for example, in the case of Ronald Hall, of which he himself has given a valuable and interesting account in the *Brit. Jl. Ophthal.*, September, 1945. He says, " I can speak from experience when I say what a terrible handicap this is for a child. Although in World War No. 1 I spent over three years at the Front, I can truthfully say that I never during those years experienced a fraction of the stark terror that I did as a boy at school during English lessons lest I should be called upon to read aloud and reveal to the whole class that I could not do so." He was taken to an oculist but the condition was evidently not recognised, as glasses were prescribed but produced no effect. He tells how he recovered spontaneously at the age of 15 and emphasizes that it was not want of intelligence on his part, as he passed first into the Civil Service as a young man.

The first account of this disability appeared in the British Medical Journal, when in 1896 Morgan[X.1] published the case of a boy of 14 who could not learn to read, though he had no difficulty with figures: the schoolmaster said of him that if the instruction had been aural this boy would have been the smartest in the school. Words written or printed seemed to convey no impression to his mind. Morgan writes to Hinshelwood, " It was your paper—may I call it your classical paper—on acquired word-blindness and visual memory published in ' The Lancet '[X.2] which first drew my attention to the subject, and my reason for publishing this case was that there was no reference anywhere, so far as I knew, to the possibility of the condition being congenital."

Hinshelwood's paper, to which Morgan refers, describes in detail several cases of acquired word-blindness in adults suffering from disease of the brain, of which the following is an interesting example, illustrating the parallel between this condition and congenital word-blindness, *i.e.*, developmental aphasia:—

" The patient, an inspector of schools, a highly intelligent and educated man, was familiar with four languages, English, French, Latin and Greek: he had become word-blind and could no longer read English. When, however, I put a Greek book into his hand, he was both surprised and delighted to find that he could read it correctly: it was evident then that so far as Greek was concerned there was no sign of word-blindness. With Latin there were evidences of partial word-blindnesses and with

French even more so. The word-blindness in English was not absolutely complete—there was no letter blindness and short words here and there could be picked out. Thus the word-blindness extended to only three of the four languages: Greek had entirely escaped. He also read numbers with fluency and correctness. He read musical notes as fluently and as correctly as ever."

We know that there are separate symbolisations for different languages, music, drawing and the like.

Two weeks after Morgan's paper in 1896, Hinshelwood published his first communication on Congenital Word-blindness in the form of a critical note, explaining some of the symptoms in the case reported by Dr. Morgan, in the light of his knowledge of the phenomena of acquired word-blindness, and four years later, in 1900, he gave the first analysis and explanation in detail of the symptoms met with in this condition in order " to establish the diagnosis on a scientific basis and to show that the difficulties encountered in teaching children so affected to read could be overcome by patient and persistent training."

Hinshelwood published his book on Congenital Word-blindness in January, 1917.

In 1901 Nettleship[x.3] having expressed his indebtedness to Hinshelwood for his exposition of the subject, gave notes of five cases of great difficulty or inability to learn to read which had come under his observation and been recognised by him clinically years earlier, though not published, notes of two of which are given. The first of these cases was a boy aged 11, who was brought to him in March, 1882, because he was extremely slow in learning to read and it was supposed that his eyes might be at fault. Immense pains had been taken in trying to teach him to read and he was very anxious to learn. Nettleship was surprised to find that his difficulty was quite as great with words of No. 10 Jaeger and even No. 16 as with No. 1. It was not want of accommodation, for neither the size of the print nor the distance at which the book was held had any influence on the result. He knew some words pretty well, but unless he recognised a word at sight, he took a very long time to spell it: if, however, he was helped by having the word spelt out to him quickly he pronounced it at once. . . .

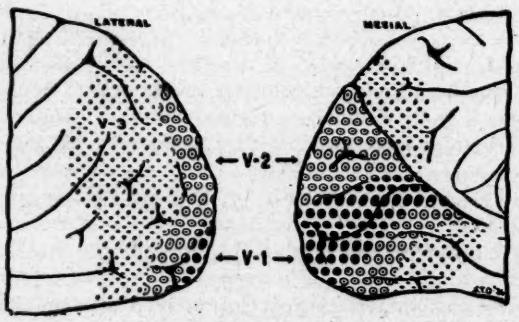
The second case, also a boy, was brought in 1882: he had great difficulty in learning to read print, though he could read music well and showed considerable facility in drawing. What puzzled his parents was that he hardly knew even short words when he spelt them: he understood what was read to him but not what he read himself. It was found in this case also that large type was not read any better than small: his manner of reading was more

suggestive of incomprehension than bad sight. After an enormous amount of patience and perseverance the boy learnt to read easily.

Nettleship finally says, " Whatever may be the anatomical cause of this condition, its importance from an educational point of view both positively and negatively is obvious. If the defect is curable, the remedy will doubtless be found in methodical and persevering instruction in reading, begun at the earliest possible age.

Although it is not intended to attempt a review of the literature on this subject, some reference must be made to the more recent work. In 1936 Professor Rönne of Copenhagen[X-4] gave an address on Congenital Word-blindness in School Children, in which he confirms Hinshelwood's experience of this disability occurring in families and refers to the case of a woman who had suffered from developmental aphasia as a child and became the mother of six children, all of whom also suffered from the same disability. He had also met with the condition in three generations of the same family. He describes his method of isolating affected children from their normal school fellows. He deplores the fact that " this quite characteristic condition is almost unmentioned in either common medical literature or in the ophthalmological."

Samuel Orton,[X-5] Iowa, U.S.A., who in 1925 had written a very interesting paper dealing mainly with Left-handedness and Mirror-reading and writing in children, published in 1937 his book, " Reading, Writing and Speech Problems in Children." This work is based upon an extensive experience in American schools and is the most detailed and authoritative account of Developmental Aphasia which has appeared.




An outline map of the lateral and mesial surfaces of the occipital region of the left hemisphere of a human brain showing the distribution of the three chief types of visual cortex. From *Reading, Writing and Speech Problems in Children*. S. T. Orton (W. N. Norton & Co., N.Y., 1937).

In describing the occipital visual centre, Orton distinguishes (1) visual perception, (2) visual recognition, (3) visual association and defines the broad outlines of the respective cerebral fields with illustrations.

His interpretation of word-blindness is an excellent extension of Head's concept of speech as " Symbolic thinking and expression." The word " Strepho-symbolia " is used by Orton to indicate a deficit in psycho-visual orientation which he was able to identify in a number of cases.[X.5a]

Emphasizing the importance of treatment in cases of developmental aphasia, Orton says: " The reading disability cases as a group form a clear-cut example of the appearance of emotional disturbances which are purely secondary to the academic obstacle. When, however, proper treatment is not instituted or the handicap is entirely disregarded because of the ' Laissez-faire ' attitude adopted by many schools, the feeling of inferiority is very apt to extend to other fields so that the child approaches every task in the expectation of failure and all of his school work may lag seriously behind." He advises, however, that " failure in learning to read with understanding must not be considered a specific disability unless it is out of harmony with the child's skill in other fields—notably the ability to learn by hearing."

The research which was initiated under the Ross Foundation in Edinburgh in 1938[X.6] was not undertaken because the subject was new, but because it had not received attention in the Edinburgh Primary Schools (the laissez-faire attitude mentioned by Orton!). While it was found in the course of these investigations that nearly 10 per cent. of children in the Primary Schools showed evidence of this disability, only about half that number required special tuition, the others recovering under the usual school training.

Miss M. Macmeeken, M.A., B.Ed., Ph.D.,[X.7] who carried out the research for the Ross Foundation, has as a psychologist been very successful in the education of children suffering from developmental aphasia: she considers the undertaking one for a specialist only: the willing co-operation of the child must be secured and subjects selected with a view to maintaining the lively interest of the pupil who takes part in the work with the teacher alternately in writing and reading. Not only is good method necessary but an extended period of time is required to secure the result. Three school terms are usually found necessary.

In considering the underlying causes of this disability it would seem to fall into two parts which, while they react upon each other, are distinct:—

(a) Mirror reading and writing, twisting of syllables and confusion of certain letters and palindromic words, relating to

insufficiently developed dominance in one of the cerebral hemispheres: these earlier manifestations (as above noted) frequently disappear in the first few years of school life.

(b) Failure in word memory, which tends to be a more permanent and stubborn difficulty to be overcome: this may relate to the delayed development of myelination of cortical neurons, with associated delayed function.

A reference to this subject of myelination occurs in a paper which appeared in the Transactions of the Royal Society of Edinburgh in 1913[X.8] by the late Alexander Bruce, M.D., LL.D., F.R.C.P.E., and James W. Dawson, M.D., from which I quote: "If it is true that every cell differentiates in view of a function, it is necessary to remember that it is the functioning which determines and perfects the cell differentiation. The nerve paths in the embryo remain as embryonic nerves till the function of the tract is called into play: influences which accelerate or retard the period at which nerve fibres are brought into functional activity have also an effect in determining the date of complete axial fibril and myelin differentiation. *Margulies*[X.9] has pointed out that in the newly-born kitten, if the eyelids on one side are carefully opened, the optic nerve on that side myelinates before that of the opposite side excluded from the light, and numerous other instances might be given where the completion of differentiation is related to the completion of function. The fibres in the distal end of a non-united nerve remain for a very considerable time as embryonic nerve fibres, but when secondary suture is carried out they very rapidly effect a complete differentiation—in a period of time in which it would have been impossible for axis-cylinders to grow out from the central to the distal end. The differentiation proceeds, therefore, *pari-passu* with the functioning which is its determining cause. Ballance and Stewart[X.10] think that some stimulus, afforded by the conducting impulses, is necessary in order to admit of the full development of the nerve fibres."

I wish here to express my indebtedness to A. Ninian Bruce, M.D., F.R.C.P.Ed., Lecturer on Physiological Neurology, University, Edinburgh, for directing my attention to the above-noted research in which he took part with his father.

In an address entitled "Some Recent Advances in the Study of the Brain as the Implement of Mind,"[X.11] Professor R. J. A. Berry, M.D., F.R.C.S., discussed myelination in the normal and the abnormal brain. This prompted me to write to Professor Berry and to look up his former work on this subject. From his book, "Brain and Mind," 1928, the following passage seemed to have a special bearing on the possible significance of myelination in developmental aphasia: "Flechsig has shown that myelination

does not occur simultaneously in all parts of the nervous system, but is later in proportion as the nerve fibre (axon of the neuron) is more recent in the phylogenetic history of the animal. Not only are the entering receptor neurons of the spinal cord more numerous than the outgoing effector neurons, but they develop or myelinate earlier, in order that they may function earlier. Generally speaking, the same holds good for the neo-pallial cerebral cortex, and the last of the cortical neurons to myelinate are those associating or linking together the association areas of the cortex, and these are precisely the areas which are universally regarded as being the seats of the higher mental processes. But if these same areas are not stimulated by suitable incoming receptor impulses, their association neurons will not myelinate and consequently the areas remain throughout life veritable " silent " areas, to the detriment of the mentality of the individual.

It consequently follows, and it is a strikingly significant fact, that the general order of acquisition of the nerve properties essential to life are :—

1. Transmission of entero-ceptise impulses from viscera by means of both non-medullated and medullated fibres through the autonomic nervous system.

2. Transmission of proprio-ceptive impulses, concerned in locomotion.

3. Transmission of extero-ceptive impulses such as touch, pressure, sight hearing, etc.

4. The last series of neurons to myelinate, that is to function, are those of the cortex which correlate and control the incoming extero-ceptive impulses, and extend them through the association areas, thus making possible education, speech thought and reason. If the neurons of this series fail to myelinate, there must follow an impairment of intelligent action and a reaction to the environment on a lower plane.

The period of time occupied by the myelination of these four great developmental series is a long one, but differs very considerably in different individuals. It commences before birth and goes on, in the educated classes, until well on into middle life, because education, that is, the constant submission of the cortical association areas to appropriate incoming receptor impulses, is a powerful stimulus to the internuncial association cortical neurons. In the non-educated classes the process of myelination of these neurons ceases much earlier in life, and as a consequence they do not attain the same degree of intellectuality.

The importance of myelination is also borne out by pathology for it is a significant fact that in *multiple* or *insular sclerosis* of the

brain and cord, the axis cylinders of the areas affected remain intact whilst the myelin sheaths are destroyed. The disturbances of co-ordination accompanying this condition may, therefore, be an expression of a loss of insulated conduction.

In considering myelination in relation to the differentiated cortical visual fields, Orton refers to Flechsig's work as follows:

"Flechsig found that maturation proceeds in three distinct waves covering, in separate stages, those areas of the brain cortex whose destruction leads to the three syndromes of cortical blindness, mind blindness and word blindness and the comparable conditions in audition. Flechsig demonstrated that at the time of birth only the "arrival platforms" or first level cortices have received their myelin, that a second period of myelinization follows during the first two or three months after birth which results in the ripening of the second zone of cortex lying near by each arrival platform and that only during the final or third wave does maturation occur in the areas of the third level."

He continues: "I have emphasized this dissection of the cerebral functions into steps because it offers us some understanding of how a selective loss of reading, for example, in the adult, or a selective retardation in learning to read in a child, may occur with full visual competence in other regards."

Developmental aphasia is an isolated disability. The diagnosis is difficult and uncertain in mentally defective children, but clearly recognisable in children otherwise normally developed in relation to age. The characteristic mental defects are related to difficulties in symbolisation and in word-memory: all other faculties of recognition and recollection are normal.

All expert and experienced teachers of such children are agreed that encouragement, patience, perseverance and time are necessary and in advancement the pupil must make the pace. In all this the most important element in securing progress lies in oft-repeated practice (in reading and writing) by performance on the part of the pupil. This activity on the part of the child fulfils the requirements of cerebral stimulation referred to by Bruce and Berry in relation to the development of function.

I suggest that the localized delay or failure in the development of myelination of internuncial nerve fibres in the cerebral cortex is the most probable explanation of this developmental failure in learning to read.

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## HISTOLOGICAL FINDINGS IN A CASE OF ANGIOID STREAKS

BY

F. H. VERHOEFF

BOSTON, MASS.

FOR the privilege of making this report I am indebted to the late Dr. Grady E. Clay. It deals with the microscopic examination of one eye removed after death from a patient with angioid streaks in both eyes. The eye was removed under the direction of Dr. Clay and sent by him to Dr. Algernon Reese for sectioning. A complete set of celloidin sections was prepared and stained under Dr. Reese's supervision and then sent to me at the request of Dr. Clay. The hospital at which the patient died was the Grady Memorial Hospital of Atlanta, Georgia, and to the authorities of this institution I am indebted for complete copies of the hospital records including the autopsy report on this patient. The clinical record was signed by Guh H. Adams, M.D. The autopsy was performed by Abner Golden, M.D., and the report signed by Walter H. Sheldon, M.D., pathologist. For the purposes of this paper the following summary of these hospital records will suffice:

The patient, a 50-year-old coloured female was admitted to the Grady Memorial Hospital, Atlanta, Ga., Jan. 28, 1944. She was known to have had syphilis which was inadequately treated. However, the Kahn test was negative at the final admission to the hospital although in 1935 the Wassermann test was 4 plus. She was known to have had hypertension since 1935. In 1939 the blood pressure was recorded as 200/110 and at this time she began to experience intermittent oedema of the ankles. There were not marked symptoms, however, until three

weeks before present admission when she became short of breath, orthopneic, and had several attacks of paroxysmal nocturnal dyspnea and a cough productive of thin white sputum. Peripheral edema became marked. The temperature was 100°, pulse 110, respiration 30, blood pressure 140/100. The patient was in respiratory distress and the neck veins were distended. There was dullness to percussion over the right lung base where many medium and fine rales were heard. The heart was markedly enlarged to the left, and there was a systolic murmur at the apex. There was a diastolic gallop. The liver was enlarged to palpation, and tender. Reflexes were normal.

Dr. Clay observed and later reported to me a fact not noted in the hospital record, namely, that the patient had pseudo-xanthoma elasticum, a condition with which he was thoroughly familiar. On ophthalmoscopic examination Dr. Clay found a few angioid streaks in both fundi. He intended to give a detailed description of the streaks, but the patient died before he could do so. He recorded in addition that "the media were clear, the nerve heads normal. The retinal arterioles showed Grade 2, arteriosclerosis, and Grade 1 angiospasms."

The patient received digitalis and other cardiac therapy, but failed to respond. She died on her seventh hospital day.

At autopsy, extensive old and recent infarcts of the lungs were found. The branches of the pulmonary artery showed old and recent thrombosis, and some showed complete recanalization. The heart showed extensive old and recent infarction, and mural thrombi, displaying varying degrees of organization were present in both ventricles. The heart weighed 580 gms. and was dilated. The aorta throughout its length displayed a rather marked degree of arteriosclerosis and numerous calcified atheromatous plaques. The viscera showed chronic passive congestion and there was extensive central haemorrhage and necrosis of the liver, and recent infarction of the spleen. Of interest also, was thrombosis of the right transverse sinus of the dura mater.

Incidental findings included leiomyomata of the uterus and a small paraovarian cyst. Microscopic examination of the heart, lungs, spleen, pancreas, liver, kidneys, showed generalised arteriosclerosis. The sclerosis included branches of the coronary arteries.

Cultures obtained at autopsy showed no growth from the lungs and coagulase negative staphylococcus aureus from the blood.

The left eye, removed 11 hours after death, was fixed in 10 per cent. formalin. The celloidin sections made horizontally through the entire eye included the whole of the optic disc and a considerable extent of the fundus above and below it. The sections were thin, well stained in alum haematoxylin and eosin, and unusually free from artefacts. After careful examination, selected sections were dismounted to me and restained by my elastic tissue stain[1] and by other methods.

The globe shows no distortion in the sections, and the choroid and retina are everywhere *in situ* except for a slight artificial separation of the retina anterior to the equator on the temporal side. The optic nerve and disc are normal. At the margin of the disc there are two large conglomerate colloid excrescences, each about 0·10 mm. in diameter, one on the nasal side in the mid-plane, the other on the temporal side below. The former contains two minute blood vessels (Fig. 1). Otherwise the retina is normal. There is marked peripheral cystoid degeneration, but this is no greater than that often seen at this age. The rods and cones show the usual distortion seen in normal eyes removed post mortem. The choroid is so slightly shrunken by the fixation that the details

of its structure are easily seen. It is normal except for the changes in Bruch's membrane next described, and a few insignificant foci of lymphocytes. The elastic tissue of its stroma is neither increased nor diminished in amount, and stains normally. The

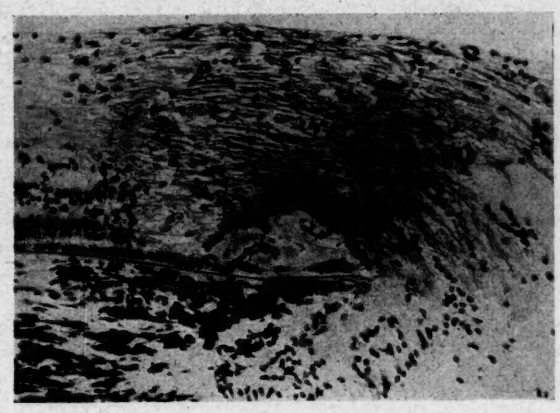

FIG. 1.

Vascularized colloid excrescence at margin of disc. The basophilic Bruch's membrane is also well shown. H. and E. Photo. ×180.

FIG. 2.

Wide gap in basophilic Bruch's membrane—oblique section of angioid streak. The pigment epithelium shows some post mortem disturbance and the chorio-capillaris is not well shown, but both are intact. A few new cells have been formed at the margins of the gap. Elastic tissue stain. Photo. ×360.

whole uvea and the sclera are more heavily pigmented than in the eye of a white person, but less so than in the eye of a pure-blooded negro.

Bruch's membrane in the posterior fundus stains strongly in haematoxylin, that is to say, is basophilic. The basophilia is continuous about half way to the equator on each side, then becomes patchy as in Fig. 2 of Verhoeff's and Sisson's paper,[2] and finally ceases near the equator. However, even where it is continuous the basophilia is not uniform, but makes Bruch's membrane appear to vary considerably in thickness at frequent intervals. This indicates that originally the basophilia was patchy here as it is now towards the periphery. On the nasal side of the eye a wide gap is seen in the basophilic membrane in every section that includes the upper half of the optic disc. Reconstructed from the sections, the gap begins at the upper margin of the optic disc, courses nasally downward and reaches the horizontal mid-plane at a distance of 4 mm. from the disc margin. Here the gap is 0·24 mm. wide in the section. Below this level the gap is no longer seen, probably because it has become horizontal. In one place in the middle of the gap a short stretch of basophilic membrane remains, as if the membrane had ruptured in two places close together. At its narrowest place the gap is 0·06 mm. wide in a section. In all sections the pigment epithelium and the choriocapillaris are intact at the site of the gap, and appear to be normal except that the epithelium shows slight post-mortem changes. In some sections these two structures are bulged slightly forward, in others slightly backward (Fig. 2) through the gap. This displacement is no doubt artificial. In a few sections there are within the gap several new formed spindle-cells just beneath the pigment epithelium (Fig. 2). Some of these are pigmented. The edges of the gap are not square, but always more or less pointed, suggesting that the gap resulted from a rupture at a relatively weak place in the basophilic membrane.

In addition to the wide gap just described, two other gaps are found in Bruch's membrane. Each of these is very minute, only 0·009 mm. wide, and is seen in only 4 consecutive sections. One is on the temporal side 0·45 mm. from the disc, the other on the nasal side 1·0 mm. from the disc (Fig. 3).

In the anterior part of the eye a pathological finding of possible importance is a localized exuberance of elastic tissue at the corneal limbus on each side in the horizontal meridian (Fig. 4). This elastic tissue is even more abundant than that generally found in a beginning pterygium, shows less degeneration than is usually found in pingueculae, and is not to any extent basophilic.

FIG. 3.
Minute gap in basophilic Bruch's membrane. H. and E. Photo. ×675.

FIG. 4.
Exuberant elastic tissue (pinguecula) at corneal limbus, nasal side. Elastic tissue stain. Photo. ×70.

FIG. 5.

Concretion in epithelium of pars plana of ciliary body. A similar concretion was found in another section. H. and E. Photo. x 152.

The cornea, iris, and lens are normal. The ciliary processes show hyaline change, consistent with the age of 50 years. Two sections some distance apart, each shows a fairly large concretion within the epithelium of the pars plana (Fig. 5). The sclera, including its elastic tissue, is normal and free from calcific deposits. The intra-ocular vessels, including those of the choroid and retina, show no definite sclerosis. Some of the choroidal arteries, owing to their post mortem collapse, appear to have unusually thick walls. The posterior ciliary vessels seen in the vicinity of the optic nerve are also free from sclerosis.

## COMMENT

The only abnormal histological findings in the fundus of this eye, aside from the two drusen at the margin of the optic disc, were the basophilia of Bruch's membrane and the gaps in this membrane. Other than the wide gaps, seen on the nasal side in the sections, there was nothing to account for the angioid streak that had been seen ophthalmoscopically. It is especially noteworthy that the pigment epithelium and chorio-capillaris were intact at the site of the gap. Allowing for the fact that the streak was sectioned obliquely, its real width was probably about 0·10 mm. to 0·05 mm. The two other gaps found were too minute to have been seen ophthalmoscopically, but probably in the course of time would have widened and lengthened. In other words, they probably indicated how angioid streaks begin.

To explain, on the basis of these findings, the ophthalmoscopic appearance of an angioid streak, one must assume that Bruch's

membrane, especially when basophilic, obscures the chorio-capillaris and contributes to the brightness of the fundus by reflecting a considerable amount of light. Within a gap, this reflection is absent, and the light is largely absorbed by the chorio-capillaris. Thus the appearance of a streak is due to increased visibility of the choroid, especially the dark red chorio-capillaris, exposed beneath the pigment epithelium at the site of a gap. This explains why in certain cases Dr. Clay has been able to obliterate the visibility of a streak by pressure upon the eye, for such pressure might express the blood from the chorio-capillaris. It is interesting that in the present case one of the sections in the middle of a gap showed an island such as occasionally is seen ophthalmoscopically in cases of angioid streaks. No doubt it resulted from Bruch's membrane rupturing at two places close together.

Böck[3], in 1938, reported the microscopic findings in two eyes, removed 48 hours post mortem, which ophthalmoscopically had shown numerous typical angioid streaks. Hagedoorn[4], in 1939, reported similar miscroscopic findings in two eyes also removed post mortem. In Hagedoorn's case the ophthalmoscopic examination was unsatisfactory, so that his microscopic findings would have been of doubtful significance were it not for the fact that they agreed with Böck's. Recently, Klien[5] has reported the microscopic findings in two eyes in which angioid streaks had been found ophthalmoscopically. Her findings were essentially the same as those described by Hagedoorn. These observers noted that Bruch's membrane stained deeply in alum haematoxylin and found breaks in the membrane. Apparently none of them was aware of the findings of Verhoeff and Sisson[2], noted below, although Hagedoorn used the term "basophilia" and found a senile eye in which this condition of Bruch's membrane existed. Böck thought that the gaps in the membrane would be ophthalmoscopically invisible if the pigment epithelium remained intact over them. Hagedoorn's explanation of the ophthalmoscopic appearance of the streaks was similar to that given above by me.

In 1928 I reported finding microscopically[6], on the inner surface of the choroid of an enucleated eye, numerous small ridges. As seen microscopically these appeared as dark streaks similar in size and distribution to angioid streaks. In addition, I found changes in the macula that seemed to accord with those often seen ophthalmoscopically in cases of this condition. I felt sure, therefore, that the ridges were angioid streaks. Since such ridges were absent in Böck's, Hagedoorn's, Klien's, and the present case, I am compelled to abandon this view and to believe that my case was a highly unusual one in which the ophthalmoscopic picture would have closely simulated that of angioid streaks. It

can now be regarded as certain that angioid streaks are gaps in an altered Bruch's membrane. Kofler[7] astutely surmised this fact 27 years ago without histological evidence, but it was never generally accepted.

Many years ago I observed that in certain eyes Bruch's membrane stained deeply in alum haematoxylin, and in 1926 with Dr. Sisson made a special investigation of this phenomenon[2]. We found it in 60 out of 600 eyes selected at random, termed the condition of the membrane basophilia, and assumed it was due to calcification. Since we found it in no eye under 48 years of age, we concluded that it was a senile condition. We also concluded that it was not necessarily related to any other pathological condition in the eye.*

Bruch's membrane is generally described as consisting of two layers, an inner cuticular and an outer elastic layer. But behind the elastic layer, and also no doubt filling its interstices, is a thin layer of connective tissue which, as I have pointed out[2], could be regarded as a third layer. Perhaps a more accurate way to describe Bruch's membrane is to say that it consists of an inner epiblastic cuticular layer produced by the pigment epithelium, and an outer mesoblastic layer composed of collagen abundantly pervaded in its inner portion by fine elastic fibrils. These fibrils are coarser near the optic disc and here extend entirely through the mesoblastic layer and continue into the underlying choroidal stroma. In thick cross sections, and often even in thin sections after formalin fixation, it is difficult or impossible to distinguish the two layers, the membrane appearing as a rather thick single layer. When the membrane is basophilic, this condition, if slight, often can be seen to involve only the elastic tissue, but if marked, it seems to involve the whole thickness of the membrane. Nevertheless even when the basophilia is marked, plane sections may show individual elastic fibrils. In its early stages the basophilia is not continuous, but is seen in cross sections in the form of long spindle-shaped spots resembling elongated nuclei. These appearances are depicted in the paper[2] referred to.

In many eyes I have found Bruch's membrane throughout its thickness abnormally eosinophilic and hyaline, and not at all

* Mrs. Helenor Wilder has recently sent me from the Army Institute of Pathology in Washington sections of five eyes with such basophilia, from patients aged respectively 39, 32, 26, 25 and 20 years. In four of the eyes the basophilia was very slight and there were no breaks in the membrane. However, angioid streaks might have developed later. The other eye (aged 25 years) shrunken and degenerated as the result of an old injury, showed marked basophilia of Bruch's membrane and breaks indicative of angioid streaks. The possibility of angioid streaks existing in the fellow eye of this patient was not excluded. It is unlikely that the degeneration of this eye was an essential factor in the calcification of Bruch's membrane, since in many other similarly degenerated eyes I have not found such calcification.

basophilic. In some eyes it is both basophilic and eosinophilic, but I have not yet determined whether it is always eosinophilic when it is basophilic. However, I suspect this to be true and that in sections stained in both haematoxylin and eosin the basophilia hides the eosinophilia. I also suspect that basophilia is always preceded by eosinophilia of Bruch's membrane. In the present case, in sections that are stained only lightly in haematoxylin it is easily recognizable that Bruch's membrane is both eosinophilic and basophilic. Unna called degenerated elastic tissue which stained in haematoxylin, elacin. It has been found this gives the differential staining reactions of calcium, and often in addition those of iron. It is evident, therefore, that basophilia of Bruch's membrane means calcification of this membrane as I originally assumed. The basophilia of elacin elsewhere, however, is seldom if ever as intense as it often is in Bruch's membrane. Böck found that in his case the membrane stained differentially for calcium but not for iron. Hagedoorn found that it stained differentially for iron but not for calcium and attributed failure of the calcium test to acidity of the formalin used in the fixation. Klien found that the membrane gave the Kossa reaction for calcium and the Turnbull blue reaction for iron.

That basophilia of Bruch's membrane sometimes occurs in senile eyes is not surprising, for degeneration and calcification are characteristic of old age. But according to Holloway[8] almost half of the cases of angioid streaks have been observed before the age of 40, and 4 cases before the age of 20. Since vision is not appreciably impaired by the condition until the onset of macular changes, no doubt many of the cases were not discovered until long after streaks had formed. Hence in cases of angioid streaks, basophilia of Bruch's membrane is not dependent upon age. Nor is it necessarily dependent upon defective calcium metabolism, for degenerated tissues readily undergo calcification even in young normal individuals. Hagedoorn assumed that the basophilia was due to " precocious senility of the elastic fibres " of the body.

Two closely related questions now arise. First, what causes gaps in basophilic membrane? Second, why are angioid streaks not associated with the basophilia that often occurs in senile eyes? The second question was not discussed by Böck, Hagedoorn, or Klien, evidently because they were unaware of the fact that basophilia of Bruch's membrane is a common senile condition. Theoretically a gap could be caused by complete dissolution of Bruch's membrane at a localized site. But microscopically there is no evidence for this. It seems certain that the membrane has ruptured and that the broken edges have separated, leaving the

other tissues apparently unaltered. Assuming, as also seems certain, that the basophilia is due to calcification, it is obvious that a basophilic membrane could be fractured by voluntary movements of the eye, winking, and " rubbing the eye " by the hands. Widening of the gaps probably results not from elasticity of the membrane, because calcification would do away with its elasticity, but from the elasticity of the choroid as a whole. Presumably this elastic tension not only widens and extends the gaps but contributed to their original cause. In senile eyes, it is reasonable to suppose that the choroid has largely lost its elasticity long before the membrane is calcified. Hence angioid streaks do not usually result when fractures of Bruch's membrane occur in senile eyes—the broken edges do not tend to separate and may even tend to override each other (Fig. 1, Verhoeff and Sisson[2]). That angioid streaks occur chiefly in the vicinity of the optic disc is no doubt explained by the fact that basophilia is always most marked here. This may be because, as I have already pointed out, Bruch's membrane is normally somewhat different in this vicinity than elsewhere. Why, in cases of angioid streaks, and in many senile eyes, this membrane alone of all structures of the choroid should undergo calcification is not obvious. Possibly this fact is partly dependent upon the close relation of the membrane to the chorio-capillaris.

A feature characteristically associated with angioid streaks is a mottled appearance of the fundus. Probably this is due to unevenness and discontinuities such as seen microscopically in the basophilia of Bruch's membrane in the present case. The marked proliferative changes within and along the gaps in three of the cases explain the white borders and ophthalmoscopic appearances of some of the older streaks. Such proliferative changes may also explain the disappearance of streaks. In none of these cases was there any reformation of Bruch's membrane.

Haemorrhages described as choroidal or sub-retinal are frequently seen in cases of angioid streaks. Since the haemorrhages often occur early in life, it seems to me probable that they are usually not due to local vascular disease, but to fracture of the calcified Bruch's membrane causing rupture of the chorio-capillaris. In some cases the rupture and haemorrhage might not result immediately from the fracture, but later from widening of a streak. If the pigment epithelium was not ruptured, the blood could lift it up in the form of a mound and later become organized into solid tissue. When occurring beneath the macula this process would result in the condition known as disciform degeneration of the macula. As first demonstrated by Verhoeff and Grossman[9] and soon afterwards but less conclusively by Braun[10],

senile disciform degeneration of the macula is typically produced by haemorrhage beneath the pigment epithelium.

In addition to the streaks, mottling of the fundus, and subretinal haemorrhages, other fundus changes often occur in cases of angioid streaks. It is believed that macular changes will ultimately occur in every case if the patient lives long enough. Only exceptionally do these macular changes take the form of the typical disciform degeneration just mentioned. In the present case the fundi, including the maculae, were normal except for the streaks. This was true also of Böck's case, with the exception that there was some slight formation of new tissue on Bruch's membrane elsewhere than in the macula. Only Hagedoorn's and Klien's cases afford histological information as to the late fundus changes. The findings in their cases were remarkably alike. In each, both maculae were involved, and in similar fashion—there was a thick layer of vascularized tissue on the inner surface of Bruch's membrane. This tissue was very old and in each case showed foci of ossification in one eye. In both cases similar tissue was also present elsewhere in the fundi. Klien described in addition, the widespread formation of a thick cuticular layer by the pigment epithelium. On the basis of her histological findings she satisfactorily accounts for the fundus pictures in five clinical cases of angioid streaks.

Aside from the streaks themselves, and possibly the deeply seated haemorrhages, none of the fundus changes seen in cases of angioid streaks is peculiar to this condition. Thus the vascularized tissue, found by Hagedoorn and Klien between Bruch's membrane and the pigment epithelium, may occur in eyes without angioid streaks, and without basophilia of Bruch's membrane. Most commonly it occurs in senile eyes, but is not necessarily associated with local vascular changes. Brown[11] has called special attention to it. Vessels enter this tissue through holes in the membrane. These holes are not due to fractures of the membrane, for usually it is not basophilic. I assume that they result from penetration of the membrane by capillary sprouts which develop into arteries and veins. Sometimes this tissue is formed beneath the macula and produces a condition that ophthalmoscopically would be difficult to distinguish from the typical senile disciform degeneration due to haemorrhage. In fact, in Hagedoorn's and Klien's cases I am unable to decide this question even by the microscopical evidence.

Since in cases of angioid streaks, cardio-vascular disease often develops, it is probable that in some of the cases disciform degeneration of the macula is dependent upon vascular disease just as it usually is in ordinary senile cases. Haemorrhages

within the retina, and circinate retinitis, occurring in association with angioid streaks, are no doubt due to vascular disease. Klien attributes almost if not all the changes in the fundi in cases of angioid streaks to calcification of Bruch's membrane. Thus she says " The clinical picture of angioid streaks represents not only the visible ruptures in Bruch's membrane but also the multiform end results of irritation of pigment epithelium and chorio-capillaris by the sharp, calcified edges and fragments of the broken membrane." With this view I cannot fully agree. For as already indicated I have seen in eyes showing no basophilia of Bruch's membrane the changes she attributes to irritation by calcified membrane. Among these changes she does not mention subretinal haemorrhage, which, as I have suggested above, may result from fracture of the calcified membrane.

In the present case at the margin of the disc there were two large " colloid excrescences " (" Drusen "), one of them vascularized. Böck and Hagedoorn also noted " Drusen " on the discs in their cases. Such formations are typically senile, that is to say degenerative in origin, but it is impossible to maintain that degeneration of elastic tissue has anything to do with them. Klien found " several hyaline bodies in the temporal half of the left nervehead." It would seem, therefore, that in cases of angioid streaks there is not only degeneration of Bruch's membrane, but sooner or later also degeneration of the pigment epithelium and various proliferative changes associated therewith. A degenerative process noted in the present case but not in the other three cases, was the formation of concretions in the pars ciliaris retinae (Fig. 5).

On each side of the eye examined in the present case there was a large pinguecula. Hagedoorn noted a large pinguecula on one eye in his case. Böck and Klien noted no pingueculae in their cases, but may not have looked for them. As a matter of fact, a section kindly sent me by Dr. Klien shows a pinguecula on the nasal side of the left eye—she did not section the anterior part of the right eye. Histologically, a pinguecula except in size is essentially identical with a lesion of pseudo-xanthoma elasticum. But since both conditions are similar to senile elastices of the skin the only relationship between them may be that both are degenerative conditions.

It is noteworthy that in all four of the cases in which the eyes have been examined microscopically, death was due to cardiovascular disease. In Böck's case the patient was a male, aged 44, in Hagedoorn's a female, aged 48, in Klien's a male, aged 53, and in the present case a female, aged 50. Pseudo-xanthoma

elasticum was absent only in Klien's case. In the present case, although there were evidences of marked general arteriosclerosis of the larger vessels, the vessels of the retina and choroid, and the posterior ciliary vessels seen in the sections, showed no definite sclerosis. Böck also found, with the exception of one choroidal artery, the retinal and choroidal vessels free from sclerosis, but found marked sclerosis of the posterior ciliary arteries. He thought that the atheromatous changes in the aorta in his case were primarily due to degeneration of elastic tissue. Hagedoorn in his case found slight thickening of the walls of the choroidal arteries but no intimal proliferation. No autopsy was done in his case. Klien's findings were substantially the same as Hagedoorn's. It would seem that in none of the four cases were vascular changes in the choroid or retina sufficiently marked to account for any other lesions in the eyes.

There are three conditions that have been associated with angioid streaks too often to be merely coincidental, namely, cardio-vascular disease, pseudo-xanthoma elasticum, and Paget's disease. Holloway[8] found that cardio-vascular disease was noted in 23·3 per cent. of the cases he collected from the literature. Actually it may have been overlooked in many of the other cases. This fact suggests that vascular disease will finally develop, and at a relatively early age, in every case of angioid streaks. Clay[12] found pseudo-xanthoma elasticum in 30 per cent. of his cases of angioid streaks. Apparently I was the first to note angioid streaks in a case of Paget's disease[6]. Twelve such cases have been reported to date but these may give an inadequate idea of the frequency of the association, for Terry[13] found three cases of angioid streaks in 22 cases of Paget's disease. Paget's disease is typically associated with general arteriosclerosis, but no case has been reported in which it was associated with both angioid streaks and pseudo-xanthoma elasticum.

It requires great stretching of the imagination to assume a common systemic cause for angioid streaks, cardio-vascular disease, pseudo-xanthoma elasticum, and Paget's disease. It is true that some of the elastic tissue in pseudo-xanthoma becomes basophilic, but there is first marked hyperplasia of the elastic tissue and this does not occur in the case of Bruch's membrane. As regards Paget's disease, Klien suggests that in this disease the angioid streaks may have a different origin, in that calcium is deposited in a normal Bruch's membrane. I can explain the associations in question only by assuming that the four conditions are independently abiotrophic and when they occur together do so as the result of hereditary linkages.

## CONCLUSIONS.

Angioid streaks result from ruptures of a basophilic Bruch's membrane. The gaps are widened by the elastic tension of the choroid. In the ophthalmoscopic picture the basophilic condition (calcification) brightens the contiguous fundus and makes conspicuous the dark red chorio-capillaris exposed beneath the pigment epithelium by the ruptures. The streaks are later often altered in appearance by proliferative changes along or within them. The similar ruptures that occasionally occur in senile eyes do not widen into visible streaks, probably because the senile choroid loses its elasticity before Bruch's membrane becomes calcified.

Other lesions that occur in the macula and elsewhere in the fundus in cases of angioid streaks are usually due to proliferative changes involving the pigment epithelium, such as occur under senile degenerative conditions. The subretinal haemorrhages in the macula and elsewhere may be due to fractures of the calcified membrane causing ruptures of the chorio-capillaris. When such a haemorrhage lifts up the pigment epithelium in the macula, " disciform degeneration " results. Haemorrhages arising within the retina, are probably explained as is also circinate retinitis, by the vascular changes that commonly occur in cases of angioid streaks.

The association of angioid streaks in many cases with pseudoxanthoma elasticum, in some cases with Paget's disease instead, and in still other cases with neither of these conditions is difficult to explain, as is also their association with cardio-vascular disease. A possible explanation is that these associations are dependent upon hereditary linkages.

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# A CONTRIBUTION TO THE MICROSCOPICAL ANATOMY OF THE SYMPATHIZING EYE

BY

R. AFFLECK GREEVES

IN comparison with the number of existing publications concerned with the microscopical anatomy of the exciting eye in sympathetic ophthalmitis, those dealing with the sympathizing eye are relatively few. In most ophthalmological text-books indeed, it is stated that the character of the histological changes found in exciting and sympathetic eyes is identical.

The subject of this communication is a number of sympathizing eyes which I have had the opportunity of examining after they had been sectioned. These are 13 in number, they have been collected from different sources, and their history, I think, leaves no doubt as to the true nature of their pathological condition; in all of them the original perforating injury to the exciting eye was an intraocular operation.

The order in which I have arranged this series of cases corresponds to the particular length of time which elapsed between the date on which inflammatory signs were first observed in the sympathizing eye and that on which it was enucleated in each case. In Case 1 this period was the shortest, and in case 10 it was most prolonged. In the 3 cases which I have placed last on the list, the exact duration of this period, although undoubtedly a long one, is somewhat uncertain.

A study of the foregoing cases shows that the particular character of the inflammatory changes occurring in sympathizing eyes is not related to the duration of the disease, and that this statement also applies to the distribution of such changes in the various ocular tissues. Nor can any relationship be found between either of these factors and the length of time elapsing between the injury to the exciting eye and the onset of inflammation in the sympathizing eye.

In 7 cases the infiltrating inflammatory cells were purely lymphocytes and plasma cells, in 6 cases epithelioid cells were present and in 3 of the latter, giant cells appeared. The only constant factor common to all these cases is the presence of an irido-cyclitis which varied considerably in character and intensity. The choroid was found to be normal in 5 cases, while in 6 cases areas of infiltration were found consisting of lymphocytes and plasma cells only. Epithelioid cells occurred in the choroid in 2 cases, and giant cells in one case only. These areas of choroidal

infiltration consisted of localized patches, always situated in the outer layers of the choroid, the capillary layer being free except in one case, No. 13, in which the whole thickness of the choroid was involved. Also the posterior section of the choroid, that immediately surrounding the optic disc, was consistently the most densely infiltrated part. Both these findings are in accordance with the conditions usually found in exciting eyes and I regard them as salient characteristics of sympathetic disease.

The vitreous showed some inflammatory cells in most cases.

The optic nerve was normal in 5 cases and oedematous in 8 cases in which the sheaths of the central vessels showed lymphocytic infiltration.

The optic nerve sheath was infiltrated in one case only and the sheaths of the ciliary vessels in 4 cases.

An interesting point is the spontaneous rupture of the lens capsule which was found in 3 cases, in none of which had there been any operative interference. In 2 of these cases, in both of which the disorganized iris and swelling lens matter were jumbled together in a necrotic mass, the intra-ocular pressure was low, while in the third the tension was raised.

Organized plastic exudate in the anterior chamber was found in 3 cases in which no operative interference had been undertaken and its occurrence does not support Fuchs' view that plastic exudation in exciting eyes affected with sympathetic disease is due to secondary infection and not part of the specific process.

In none of the cases did such infiltration as was present in the iris show any particular tendency to be situated in the posterior layers, and no Fuchs-Dalen bodies were seen.

From a study of these 13 cases I think it is reasonable to draw the conclusion that no special characteristic of the sympathetic inflammatory process is invariably found in the sympathizing eye on microscopical examination.

*Case* 1. Male, age 60 years. Signs of sympathetic uveitis were observed 5 weeks after operation on the other eye. Enucleation was performed 3 months later because the eye became glaucomatous and painful.

*Microscopical appearances.*—Scattered nodular lymphocytic and plasma cell infiltration of the iris, with a few epithelioid cells in some of the nodules. Slight lymphocytic infiltration of the ciliary body. The anterior uveitis was not plastic in character. Nodular lymphocytic and plasma cell infiltrations were present in the outer layers of the choroid in the neighbourhood of the optic disc. No epithelioid or giant cells were seen. Retinal vessels, optic disc, vitreous and ciliary vessels and nerves were free from infiltration.

*Case 2.* Female, age unknown. Signs of sympathetic uveitis appeared 2 months after operation on the other eye and an iridectomy was performed for the relief of secondary glaucoma. The eye was enucleated 3½ months after the first appearance of inflammatory signs.

*Microscopical appearances.*—A layer of lymphocytes was present on the posterior corneal surface, and nodular lymphocytic infiltration of the iris and ciliary body;

*Photo by E. V. Willmott*

FIG. 1.

Showing nodular lymphocytic infiltration in the posterior layers of the choroid in Case 1. The retinal detachment is an artefact.

*Photo by E. V. Willmott*

*FIG. 2.*

Showing the ruptured lens capsule in Case 3, and the invasion of the lens substance by inflammatory cells.

no epithelioid cells were seen. There is slight lymphocytic infiltration of the choroid near the optic disc. The central vessels and larger retinal vessels show marked lymphocytic infiltration in their sheaths. The ciliary vessels also show some lymphocytic infiltration. There is scattered lymphocytic infiltration in the vitreous.

*Case* 3. Female, age 49 years. Signs of sympathetic uveitis were observed 3 months after operation on the other eye, and 5 months later the eye was enucleated because of secondary glaucoma.

*Microscopical appearances.*—Dense coagulum was present in the anterior chamber and dense infiltration, mainly lymphocytic, in the iris, with a few epithelioid and giant cells in the denser nodules. There is much plastic exudation, with an organized membrane in the pupil. The ciliary body shows dense lymphocytic infiltration with a few epithelioid cells. Localized patches of plasma cells, lymphocytes, and a few epithelioid cells occur in the outer layers of the choroid near the optic disc. There is some lymphocytic infiltration round the central vessels. The ciliary vessels and nerves also show some perivascular infiltration. The optic nerve and its sheath are also invaded by lymphocytes The lens capsule is ruptured, with invasion of the lens substance by inflammatory cells.

*Case* 4. Male, age 60 years. Signs of sympathetic uveitis were observed 2 months after operation on the other eye. Enucleation took place 5 months later because of secondary glaucoma, for which a paracentesis had already been performed.

*Microscopical appearances.* Plastic exudate, partly organized, is present in the anterior chamber. Lymphocytic and plasma cell infiltration only is seen in the iris and ciliary body. The choroid and optic nerve are normal. The vitreous is slightly infiltrated anteriorly.

*Case* 5. Female, age 54 years. Signs of sympathetic uveitis were observed 3 months after operation on the other eye. 10 months later the eye was enucleated because of secondary glaucoma for which a paracentesis had already been done. Dense lymphocytic and plasma cell infiltration occur in the iris and ciliary body, and a similar type of nodular infiltration is seen in the outer layers of the posterior choroid. The optic disc shows infiltration with lymphocytes anteriorly and there is lymphocytic infiltration of the sheaths of the larger vessels. No epithelioid or giant cells are observed. No ciliary vessel or nerve infiltration is seen. The vitreous shows a few scattered inflammatory cells.

*Case* 6. Female, age 59 years. Sympathetic uveitis was observed 1 year and 5 months after operation on the other eye, and 11 months later, when the eye was shrinking it was enucleated. The iris and ciliary body are mainly disorganized, and represented by a mass of granulation tissue containing lymphocytes, plasma cells, epithelioid and giant cells. The choroid shows localized areas of lymphocytic infiltration posteriorly, but no epithelioid or giant cells. The optic disc shows lymphocytic infiltration in the sheaths of the central vessels. The sheaths of the ciliary vessels and nerves are also infiltrated. The vitreous is detached and infiltrated. The lens capsule is ruptured.

*Case* 7. Male, age 70 years. Sympathetic uveitis was first observed a year after operation on the other eye. Enucleation took place a year later because of secondary glaucoma.

*Microscopical appearances.*—Plastic exudation almost fills the anterior chamber, but some K.P. can be seen. The iris and ciliary body show scattered infiltration, with lymphocytes and plasma cells. In the posterior part of the choroid are localized patches of lymphocytes and plasma cells, but no epithelioid cells. The optic disc, central vessels, and ciliary vessels and nerves are normal. A few inflammatory cells are seen in the vitreous.

*Case* 8. Female, age 64 years. Signs of sympathetic uveitis were observed 5 months after operation on the other eye. 1 year and 3 months later, the eye was enucleated because of secondary glaucoma, for which a paracentesis had already been performed.

*Microscopical appearances.*—Organized exudate is seen in the anterior chamber. The iris and ciliary body show nodular infiltrates with lymphocytes and plasma cells, but no epithelioid cells. The choroid is normal. The optic nerve is cupped

and atrophic with a few lymphocytes in the sheaths of the larger vessels. The ciliary vessels, nerves and vitreous are normal.

*Case* 9. Male, age 70 years. Signs of sympathetic uveitis were observed 4 months after operation on the other eye. Enucleation took place 16 months later.

*Microscopical appearances.*—Nodular infiltration of the ciliary body and iris, with lymphocytes and plasma cells, and epithelioid cells, but no giant cells are seen. The choroid, ciliary vessels and nerves are normal. There is some infiltration of the larger vessels on the optic disc and some inflammatory cells in the anterior vitreous.

*Case* 10. Age, sex, and other particulars unknown. Enucleation took place 18 months after operation on the other eye. The eye was then shrinking.

*Microscopical appearances.*—Coagulum was present in the anterior chamber. The iris and ciliary body were mainly disorganized and showed dense lymphocytic and plasma infiltration with some epithelioid cells. No giant cells were seen. The choroid and optic nerve were normal as well as the ciliary vessels. The lens capsule was ruptured.

*Case* 11. Female, age 50 years. The dates are uncertain, but the eye was excised over 4 years after the operation on the other because it was then blind and painful. The iris and ciliary body show nodular lymphocytic and plasma cell infiltration, with no epithelioid cells. The choroid is normal. The optic nerve and the sheaths of the larger vessels are infiltrated anteriorly. The ciliary vessels and nerves are free from infiltration. The vitreous shows many inflammatory cells.

*Case* 12. Female, age 67 years. The eye was enucleated 9 years after operation on the other eye, because it became blind and painful.

*Microscopical appearances.*—The iris and ciliary body are slightly infiltrated with lymphocytes and plasma cells, polymorphonuclears are visible in the anterior chamber. Some nodular lymphocytic infiltration occurs in the posterior part of the choroid in its outer layers. The vitreous is clear. The optic nerve was not seen.

*Case* 13. Female, age 55 years. A left iridectomy was performed. The right

*Photo by E. V. Willmott*

FIG. 3.

Section showing the choroid in Case 13. Dense infiltration with lymphocytes and epithelioid cells. The retinal detachment is an artefact.

eye became painful and glaucomatous some weeks later and was trephined 4 months after the original operation on the left eye. It was enucleated a month later.

*Microscopical Sections.*—This eye is the only one of the series which shows all the characteristics recognized as peculiar to advanced sympathetic disease in an exciting eye. The whole of the uveal tract is a mass of granulation tissue in which all types of inflammatory cell are seen, and which shows nodules containing epithelioid and giant cells. The central vessels, optic disc, and the nerve sheath, as well as the ciliary vessels and nerves, are infiltrated with lymphocytes. The lens capsule is ruptured, but in this case the rupture may have occurred when the operation for the relief of secondary glaucoma was performed.

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## THE OFF/ON-RATIO OF THE ISOLATED ON-OFF-ELEMENTS IN THE MAMMALIAN EYE

BY

RAGNAR GRANIT

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IN this communication I would like to draw attention to some aspects of the micro-electrode work with the retina of the dark adapted decerebrate cat which have come to the fore after the appearance of my (very much delayed) summary in 1947. Some new results and concepts have emerged from the further analysis of several hundred isolated fibres in this retina and it is possible that there is something in this work that may interest the clinician also. It is not my intention to review experiments published elsewhere, except in so far as they are necessary for this discussion of concepts and principles.*

The retinal elements are either *on-elements*, *off-elements* or *on-off-elements*. The on-elements respond to light with a stream of impulses, the off-elements with a discharge at the cessation of illumination and the on-off-elements combine these two properties. For the discrimination of light and colours the on-off-elements must be the most important ones. In the cat's eye they are also the most numerous ones; there Miss Tansley and I found 80 per cent. on-off-elements. The on-elements turned up in 16 per cent. of our total of 164 elements. We have reasons to believe them to be pure rod-elements. The on-off-elements may differ in colour sensitivity at " on " and " off." For this reason it is impossible to assume that the on and off-components are set up by identical

* The original papers will be found in the *Jl. Physiol.*, and *Jl. Neuro-Physiol.*, for 1947. The latest one is due to appear in the latter Journal within a few months. The summary referred to is " Sensory Mechanisms of the Retina," Oxford Univ. Press, 1947.

receptors. Hence the on-off-element is a complex structure to which receptors of different properties have contributed. Some of them must have arrived over internuncial channels involving the retinal synapses. One of the first tasks in retinal physiology is to find out how internuncial activity modifies the primary receptor response. (The latter probably appears in a relatively pure state in the simple on-elements.) For this analytical work it is necessary to develop methods and concepts.

One of the fundamental new concepts is the off/on-ratio. Miss Tansley and I discovered this variation in the properties of the on-off-elements. We increased the strength of the light gradually and found that sometimes the on-, sometimes the off-component of an on-off-element turned up first. An on-off-element is thus relatively more on-sensitive *or* relatively more off-sensitive. Sometimes the on- and off-components were equally light-sensitive at the threshold and then the off/on-ratio obviously is 1·0. Dr. Gernandt and I have since, independently and together, measured the off/on-ratios for a large number of on/off-elements, stimulating with different wave-lengths. One obtains statistical distribution curves showing that the majority of the elements have off/on-ratios varying from 0·1 to 10·0 but that the extremes of the curve are represented by variations as large as 1000 and 0·001. This, of course, is an amazing variation and one may well ask what purpose it serves.

In a general way one can say that the variation in the off/on-ratios improves discrimination. Most acts of discrimination presuppose a moving eye for which the off-discharge is just as important as the on-discharge. A wide range of variation in the off/on-ratio increases the local variability necessary for discrimination.

In his extensive material Gernandt (unpublished) also has measurements for red (0·650 $\mu$), green (0·510 $\mu$) and blue (0·460 $\mu$) light. Any wave-length may have any off/on-ratio but the probability that the maximum would be in the green was only 0·18 as against 0·39 for the blue and 0·47 for the red light. This means that there are several elements which become relatively more off-sensitive towards either or both ends of the spectrum. Others have a constant off/on-ratio throughout the spectral range. This, of course, is a very interesting finding. My measurements of the spectral sensitivity of dark adapted cats were always carried out with the on-components, when on-off-elements were localized by the micro-electrode. They gave, when averaged, roughly the visual purple distribution of spectral sensitivity (as again confirmed in this laboratory). The off-components (which at present are being measured) cannot do so unless the element is of the type for which

the off/on-ratio is constant throughout the spectral range. Other receptors than those activated by visual purple must therefore contribute relatively more to some off-components. These apparently contain a greater number of cones than the on-components. This conclusion was also reached by Miss Tansley and myself who found that red-sensitivity tended to increase with off-sensitivity.

Another of Gernandt's results was still more interesting. He found, as I had done before, that different on-off-elements are differentially sensitive to adaptation with red, green or blue light. But to this he added the important observation, that, in general, selective adaptation of an on-off-element tended to depress the more sensitive component relatively more, so that if the element was more off-sensitive, the off-component was relatively more depressed and, *vice versa*, if it was more on-sensitive. What this means is best understood with the aid of an example. Assume that the eye be stimulated with a blue stimulus. Then, during illumination, all the specific blue-sensitive on- and off-components become depressed. The off-discharge that follows upon cessation of stimulation will therefore be favoured in off-sensitive elements containing other components than blue ones. This is precisely the kind of arrangement that would facilitate a contrast mechanism operating with on-off-elements.

Let us now consider why the off/on-ratio varies as it does. The fact itself seems rather remarkable. All receptors are working at their maximum capacity because the eye is fully dark adapted. How then is it possible for some to be a 1,000 times less sensitive than others? The on-component may be 1,000 times more sensitive than the off-component and, *vice versa*, the off-component 1,000 times more sensitive than the on-component. The off/on-ratio may thus vary from 1000 to 0·001. This occurs despite the fact that hardly any elements are likely to be *pure* cone-elements. There is always a great deal of convergence of rods and cones towards the ganglion cell from which the micro-electrode picks up the response. The rods will dominate in dark adaptation.

Nevertheless the assumption that the variation in the off/on-ratio really expresses a variation in the cone/rod-ratio deserves to be examined. If true it would mean that the less sensitive component is dominated by cones. Thus, when the off/on-ratio is high, the on-component would contain the cones, when the off/on-ratio is low the cones would be in the off-component. Available evidence does not support this simple explanation. On the contrary, the higher the off/on-ratio, the greater, on an average, the relative sensitivity to red light (0·650$\mu$) for *both* the on- and the off-component. This was found by Miss Tansley and myself

with 61 on/off-elements. At the wave-length 0·650$\mu$ the photo-sensitivity of visual purple is of the order of 0·3 per cent. of its maximum around 0·500$\mu$ so that a positive correlation between off/on-ratio and red-sensitivity can only mean that the higher the off/on-ratio the more likely that cones participate in the response.

There is another very potent argument against the idea that the off/on-ratio would be a variable illustrating merely the relative contribution of cones to the on- and off-components of the elements. This presupposes that the off/on-ratio would be constant but actually it is only constant just at the threshold and, above it, and is subject to great fluctuations under the influence of light-stimuli. Electrical stimulation of the eye also changes the off/on-ratio at the threshold. Now this is not surprising. Stimulation with light produces differences of electrical potential across the retina so that if this influences the off/on-ratio, direct electrical stimulation must do so too. The curves illustrating impulse frequency against stimulus intensity also demonstrate variations in the off/on-ratio. Sometimes the on-effect is inhibited within a certain range of intensity, sometimes the off-effect (Granit, *Jl. Physiol.*, 1944, Vol. CIII, p.103). Impulse frequency is by no means a simple function of stimulus intensity when one records from a single fibre *after* the effect has passed through a nervous centre. The optic nerve, of course, is really a central tract and this accounts for the difficulties in interpreting the message. It has already become highly differentiated. The frequency-intensity function has become modulated in the retinal centre.

With these facts at our disposal we can readily understand that the variation in the off/on-ratio at the threshold represents the selection of one particular state of balance between the forces of excitation and inhibition (or suppression) in the retina. This conclusion leads to the novel and somewhat radical concept that an element, already at the absolute threshold, is subject to " internal tension " exerted by forces of facilitation and depression. The synaptic organization maintaining the element in a resting retina (at the absolute threshold) cannot be regarded merely as an anatomical distribution pattern of the paths of various receptors, bipolars, amacrines and horizontals but it is also a structure using energy in order to suppress the activity of certain cells and, perhaps, heighten that of others. The threshold variations in the off/on-ratio demonstrate how this semi-stationary state of balance of forces within an on-off-element is organized at one particular level of intensity.

It would not surprise me if the extremes represented less probable labile states. I have seen several on-off-elements with off/on-ratios of the order of 0·001 under the influence of electrical

polarization acquire an off/on-ratio of around 1·0. This change has been in the nature of a release of the suppressed component under the influence of the electrical stimulus. The latter has been delivered from electrodes on opposite sides of the bulb.

Long ago Dr. L. A. Riddell and I myself (*Jl. Physiol.*, 1934, Vol. LXXXI. p. 1) noted with the frog's eye that a light adapted retina was a relatively more negative retina (inside more negative to outside of bulb) and pointed out that light adaptation involved slow electrical changes altering the " state " of the retina. In a later summary I spoke of " electro-adaptation." It will now be necessary to return to similar problems with the mammalian eye.

It is highly probable that the slow electrical changes induced by light determine the off/on-ratio because electrical stimulation strongly affects this relationship. But recent observations from experiments now in progress have led me to suspect that we are allowing ourselves to be too dogmatic when tacitly assuming that the anatomical organization is fixed and unchangeable. I believe that we must seriously consider the possibility that the " boutons " at the synapses expand or contract so as to alter the contact surface. In certain types of on/off-elements I find that stimulation with light induces large changes of electrical threshold. These often return very slowly and sometimes the responses to anodal and cathodal currents and those to illumination at " on " and " off," shift relative to one another in such a manner that one must raise the question as to whether one really is dealing with the same anatomical organization.

On the whole I feel that one should not be afraid of putting radical views to the test of an experiment. It seems to me a greater mistake to assume that a new technique, such as the micro-electrode technique, must necessarily answer questions suggested by the very different psychophysical method of approach. If we frame our questions on the basis of old findings the new technique may refuse to answer them. Our aim must be to put the right questions to the micro-electrode.

# THE PRESENT POSITION OF THE PROBLEM OF THE INTRA-OCULAR FLUID AND PRESSURE

BY

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ALMOST half a century ago when Parsons was working on the problem of the intra-ocular pressure, a change in the conception of the nature of the aqueous humour was emerging. Previously —without firm experimental evidence—the aqueous was generally accepted as being a secretion: it was of "vital" origin and in an age of dogma it was accepted as such. With the growth of the mechanistic conception of biology which characterised the end of the last century, however, and stimulated particularly by Starling's work on the body-fluids generally, Parsons, in conjunction with Henderson and Starling in England, concluded that the aqueous, like the tissue-fluids elsewhere, was a simple filtrate governed by hydrostatic and osmotic forces. A quarter of a century later advances in experimental technique, particularly in the physico-chemical approach to biological problems, made it clear that a conception so simple would not suffice. The chemistry of the aqueous was found to be incompatible with such an origin, and a new theory was introduced that this fluid was a dialysate in thermo-dynamical equilibrium with the blood and that upon it a through-and-through circulation was superimposed by pressure-differences at two points of its most intimate association with the blood—the ciliary capillaries and Schlemm's canal.

Such a theory has very special requirements:—

(*a*) The intra-ocular pressure (I.O.P.) should be determined by the mean level of the capillary pressure (C.P.) less the colloid osmotic pressure of the plasma proteins (O.P.), *i.e.*, by the relationship:

$$C.P. - O.P. = I.O.P.$$

With an average value of 20 to 25 mm. Hg for the intra-ocular pressure and a figure of 28 mm. Hg for the colloid osmotic pressure of the plasma proteins, the theory therefore demands a mean level of capillary pressure of about 50 mm. Hg. As a corollary to this relationship a rise in the level of capillary pressure should be reflected in a rise in intra-ocular pressure, whilst a rise in the colloid osmotic pressure of the plasma should lower the intra-ocular pressure.

(*b*) A fluid formed by filtration from the blood plasma and retained for some length of time in the chambers of the eye is not only an ultra-filtrate but a dialysate, *i.e.*, it has had time to

come into thermodynamic equilibrium with its parent plasma supposing that this equilibrium had not been established at the moment of filtration. The Gibbs-Donnan equilibrium should therefore apply to the aqueous humour and plasma: this requires that the concentrations (or activities) of all non-electrolytes capable of penetrating from the plasma into the aqueous humour be equal in the two fluids. The following relationship should apply to the distribution of the univalent ions:—

$$\frac{[\text{Concent. of Na in Plasma}]}{[\text{Concent. of Na in Aqueous}]} = \frac{[\text{Concent. of Cl in Aqueous}]}{[\text{Concent. of Cl in Plasma}]}$$

From this it follows that the osmotic pressure of the plasma should be greater than that of the aqueous humour.

(*c*) A rise in the concentration of one of the constituents of the blood, (*e.g.*, sugar), or the introduction of a diffusible foreign substance into the blood should be followed by diffusion of the substance in question into the aqueous humour in accordance with Fick's Law, *i.e.*, at a rate proportional to the difference in the concentrations in the two fluids. The relative rates at which various substances enter the eye under these circumstances would be a characteristic of the "Blood-Aqueous Barrier." It should be noted that the complete impermeability of the barrier to certain substances is not inconsistent with the dialysis theory.

These are the main demands of the theory and we have indicated that fifteen years ago there was no serious discrepancy between theory and experimental fact. The same evolution, however, has repeated itself in scientific progress. Further factual experimental results obtained by more exact and elaborate techniques have appeared: these have again rendered a relatively simple and apparently satisfactory theory inadequate. And when any theory—no matter how simple and satisfying—fails to accommodate new facts determined by newer and better methods of experimentation, the theory—no matter how useful it may have appeared—must be sacrificed. Just as Newton's Theory of Gravitation gave place to Einstein's Theory of Relativity, so the theory of dialysation must give place to something else. Unfortunately the phase of transition from one conception to another is usually a period of some confusion, and for this reason it may be of value to assess the present position and to indicate the possible direction of progress.

## EXPERIMENTAL FINDINGS

Some experimental facts will now be recapitulated.

1. *The Distribution of Sodium and Chloride.*—Van Slyke calculated that the ratio ($R_{Na}$)—concentration of Na in plasma/concentration in a dialysate—should be 1·04, the corresponding ratio

for chloride ($R_{Cl}$) being 0·96. Recent studies from this laboratory (Davson, Duke-Elder and Benham, 1936; Davson, 1939; Davson and Weld, 1941; Hodgson, 1938) have partly confirmed and partly disproved the existence of a Donnan equilibrium in this regard. Thus in cats the value of $R_{Na}$ is 1·03±0·004; $R_{Cl}$ is 0·945. In the dog $R_{Na}$ 1·04±0·004, *i.e.*, it agrees exactly with Van Slyke's theoretical requirement. $R_{Cl}$, however, is grossly aberrant, being on the average 0·92, extreme values as low as 0·89 having been observed. Chloride is thus not in equilibrium with the blood plasma, its concentration in the aqueous humour being too high. The position, however, is complicated by the fact that recent studies on dialysis with collodion membranes indicates that Van Slyke's theoretical ratios may be wrong. Greene and Power (1931) and Ingraham, Lombard and Visscher (1933), for example, obtained results which indicate that $R_{Na}$ should be nearer 1·08 than 1·04 and that $R_{Cl}$ should be in the region of 0·99 rather than 0·96. If this is true the observed values of $R_{Na}$, namely 1·03 in the cat and 1·04 in the dog, are no evidence for equilibrium but rather of the existence of an excess of sodium in the aqueous; similarly the observed value of $R_{Cl}$ of 0·945 and 0·92 indicate an excess of chloride in the intra-ocular fluid. By dialysing aqueous humour against plasma from the same animal it has been shown in our laboratory (Davson, Duke-Elder and Maurice, 1948) that sodium and chloride do actually migrate from aqueous humour to plasma to give final equilibrium ratios of 1·06 to 1·07 for sodium and 0·98—0·99 for chloride. There is thus no doubt that the sodium and chloride of the aqueous are not in thermodynamic equilibrium with these substances in the plasma.

Here, however, we are not certain that all the circumstances have been taken into consideration. Thus it is known that the aqueous contains a higher concentration of lactic acid than the blood of the jugular vein (an excess of 1·7 millimoles per litre, Fischer, 1931), due, presumably, to the formation of this substance as a metabolite by the lens and retina. Some part of the excess of sodium in the aqueous might be fairly accounted for by its combination with lactic acid (1·7 out of a total excess of about 3·0 millimoles per litre): the remaining moiety is not accounted for—nor can the excess of chloride be explained on a similar basis, and since it persists in the aphakic eye any metabolic influence of the lens must be ruled out. Some activity in respect of sodium and chloride other than dialysis must therefore exist.

A further complicating factor is the entrance of sodium and chloride into the posterior segment of the eye. It has been shown from this laboratory (Davson, Duke-Elder, Maurice, Ross and Wooden: in press), by the use of tracer elements, that sodium

(and potassium) do not penetrate into the vitreous chamber from all the vascularised tissues as do substances like glucose and thiocyanate, but enter essentially through the ciliary region. In this, as we shall see in a moment, there is an analogy with the cerebral circulation; but from the point of view of the immediate argument, this fact reinforces the argument for a special mechanism for the transference of these substances through the blood-aqueous barrier and localises it (largely, at any rate) to the ciliary region. Not only must we therefore postulate some mechanism of transfer for electrolytes differing quantitatively from simple ultra-filtration or dialysis, but we must also admit the existence of qualitative regional differences in the operation of this mechanism.

II. *Reducing Substances*: *Carbohydrates*.—The distribution of sugars is somewhat simpler. If the concentration of reducing substances (glucose) in the aqueous is estimated it is found to be lower than that in the plasma, while that in the vitreous is lower still. In the cat, for example, the relative values have been found in this laboratory to be: arterial plasma 108, aqueous 82·5, vitreous 57 (Davson and Duke-Elder, 1948; see also Adler, 1930). Regarded superficially it might be said that a theory of simple dialysis requires these values to be equal; but the deficiency in the aqueous is approximately equal to the glucose uptake of the lens, and that in the vitreous to the metabolic requirements of this tissue and the retina. That this explanation actually accounts for the deficiency is suggested by the fact that it largely disappears, so far as the aqueous is concerned, in the aphakic eye (when the concentration of sugar in the aqueous approximates that in the plasma), and becomes very much greater in the posterior segment if an excised eye is incubated so that the retinal metabolism is maintained and the alternative sugar supply by the blood cut off (when the retina will consume more sugar) (Davson and Duke-Elder, 1948). It is interesting that the concentration of glucose in the cerebrospinal fluid is very low, about the same as that in the vitreous body: in the brain conditions are very similar to those in the posterior segment of the eye.

Moreover, a study of the kinetics of the entry of carbohydrates into the eye has shown that this class of substance passes the blood-aqueous barrier at relative speeds which suggest a simple physical diffusion depending on the size of the molecules concerned (Davson and Duke-Elder, 1948). Thus pentoses (xylose) and hexoses enter the aqueous at about the same rate, disaccharides (sucrose) at a rate about one-seventh of this and polysaccharides (raffinose, inulin) at a barely measurable rate. This would suggest a simple diffusion through pores of a limiting size slightly larger than the molecules of sucrose; and the fact that natural sugars (glucose) enter at the same rate as synthetic sugars of comparable

molecular size (3-methyl-glucose, which is not phosphorylated *in vivo*) would seem to preclude any secretory mechanism so far as this type of substance is concerned. Into the vitreous body the rate of entrance is much slower, suggesting a quantitative difference in the posterior segment of the eye; and the fact that pentoses and hexoses enter at somewhat different rates into the vitreous body may indicate the presence in this region of a qualitatively different mechanism which can exert a chemical as well as a physical differentiation.

III. *Nitrogenous Substances.*—The case of nitrogenous substances is peculiar. As long ago as 1933 Adler drew attention to the fact that the concentration of urea in the aqueous humour was definitely below that in the plasma: according to his figures the concentrations in aqueous and plasma in the cat are 46·3: 54·9, that is, there is a difference of 0·0014 M. The subject has been investigated in greater detail subsequently in Adler's laboratory as well as in ours and at Boston (Adler, 1933; Kinsey and Grant, 1942; Benham, 1937; Scheie, Moore and Adler, 1943-7; Kinsey and Robinson, 1946; Ross, unpublished). The observed ratio depends in a considerable measure on the chemical methods of estimation; thus Kinsey and his co-workers claimed one ratio only to alter it as a result of applying another chemical method: with a conductivity method Benham from this laboratory obtained a ratio of 0·8 to 0·95 in the rabbit and 0·9 to 0·95 in the cat: whilst with the Conway method, Ross, working in our laboratory, has recently obtained a ratio in the cat of 0·81. There is no doubt, however, that urea is present in lower concentration in the aqueous humour than in the blood plasma. Accurate studies of other organic compounds such as amino-acids and creatinine have not been reported and would probably mean little owing to the unspecificity of the chemical methods employed: what evidence we have obtained in recent permeability studies suggests that there is a deficiency of these compounds in the aqueous humour. Again, this deficiency cannot be explained by a theory of dialysis; nor can metabolic consumption provide a reason for the discrepancy. It has been found in this laboratory, however, that not only urea, but all nitrogenous substances such as creatinine, and amino acids as glycine and alanine with their relatively small molecules, penetrate the blood-aqueous barrier very slowly and with difficulty (at about 1/3 the rate of the large-moleculed sugars) (Davson, Duke-Elder, Maurice, Ross and Woodin, in press). It is obvious that if there is a relatively easy exit from the eye by fluid in bulk and a preferentially difficult entrance of these substances, they may for purely physical reasons be in constant deficit in the " steady-state " of normal conditions (Kinsey and Grant, 1942-4; Duke-Elder and Davson, 1943; Bárány and Davson, 1948).

It is interesting that sucrose injected into the blood stream tends to distribute itself between aqueous humour and plasma so that at equilibrium its concentration in the aqueous humour is only about half that in the plasma (unpublished). Sucrose penetrates from blood to aqueous humour very slowly indeed, much more slowly than even urea, and should, by the same explanation, have a distribution at equilibrium at the "steady-state" such that the ratio of the concentrations in aqueous humour and plasma is smaller than that for urea; this has, in fact, been found (unpublished). The finding of a deficiency of a substance in the aqueous humour is no evidence of itself in favour of a secretory origin of this fluid, as has been argued (Adler, 1933).

It has been known for some time that the concentration of ascorbic acid (vitamin C) in the intra-ocular fluid is considerably greater than that in the blood plasma: this difference is much more marked in some animals (*e.g.*, rabbit and ox) than in others (*e.g.*, the cat and dog). There are at present two schools of thought as to the cause of this excess of ascorbic acid: Müller and Buschke (1934) showed that in the aphakic eye the difference in concentration was very considerably less and brought forward evidence purporting to prove that the lens actually synthesised the vitamin (Müller, 1935). Friedenwald, Buschke and Michel (1943), on the other hand, regard the high concentration as evidence of secretion by the ciliary body and in a recent study Kinsey (1947) certainly supported this hypothesis by showing that ascorbic acid, injected into the blood, passed into the aqueous humour in spite of the fact that the concentration was higher than in the plasma. If, however, the lens synthesised ascorbic acid, it would continuously pass into the aqueous humour and thence into the blood stream by simple diffusion: increasing the blood concentration would lower the rate of loss from the aqueous humour and thus allow the ascorbic acid concentration to pile up to a greater extent. The matter clearly merits further investigation.

IV. *Osmotic Pressure.*—Our early studies on the osmotic pressures of the aqueous humour and plasma (Benham, Davson and Duke-Elder, 1937) indicated that there was an excess of osmotic pressure in the plasma as compared with the aqueous so that the requirements of the dialysis theory appeared to be met. More recent work from the same laboratory (Benham, Duke-Elder and Hodgson, 1938), however, has shown that when ether anaesthesia, which raises the osmotic pressure of the plasma, was avoided, the osmotic pressure of the aqueous humour was always greater than that of the plasma, a difference in osmotic pressure in the opposite sense from that required by the Donnan equilibrium. This finding has been confirmed by Roepke and Hetherington (1940) who have shown also that the excess of osmotic pressure in the aqueous humour could be abolished by poisoning the eye with an intra-ocular injection of mercuric chloride. The finding that when aqueous humour is dialysed against plasma there is a decrease in conductivity of the former fluid (Davson, Duke-Elder and Maurice, 1948) corroborates these later findings and indicates that the excess of osmotic pressure is at least in part due to an excess of electrolyte in the aqueous humour. Analyses of the concentrations of non-electrolytes certainly indicate that they are unable to contribute to an excess of osmotic pressure in the aqueous humour; in fact, they must cause a material deficiency. A rough estimate indicates that the deficiency of sugar, urea, creatinine, amino-acids and protein

would amount to about 4·5 millimoles per litre; consequently, if the osmotic pressure of the aqueous humour is to be actually greater than that of plasma, an excess of at least some 4·5 millimoles of some other material, presumably salt, would be necessary. The dialysis experiments described above indicate that the concentration of sodium in the aqueous humour is about two per cent. higher than the equilibrium concentration, *i.e.*, there is an "excess" of about 3·0 millimoles per litre. The excess sodium ions must, of course, be accompanied by negative ions and if these are monovalent (*e.g.*, chloride) this would demand a further 3 millimoles per litre. The excess sodium in the aqueous humour can thus fully account for the deficiencies of organic substances such as sugar and urea, in fact, it is sufficient to reverse the osmotic relationships between a dialysate and plasma causing the osmotic pressure of the aqueous humour to be the greater. It may be that the maintenance of this osmotic gradient is of considerable importance in the mechanism of the intra-ocular pressure.

V. *The Intra-ocular Pressure.*—It has frequently been said that the absence of an invariable and proportional variation in the intra-ocular pressure in response to changes either in the blood pressure or the colloid osmotic difference between plasma and aqueous is incompatible with a dialysation theory. The classical researches of Parsons (1904—8) and Henderson and Starling (1904) have shown that the intra-ocular pressure does indeed follow the arterial in sudden changes in experimental animals; the more recent work of Duke-Elder (1926—30) has confirmed this. This, however, applies only to dramatic experimental changes. It must be remembered that the intra-ocular pressure will vary with the capillary pressure. It has not been possible to measure the capillary pressure directly in experimental investigations of this problem and one has had to assume that a rise in arterial pressure would be reflected in a rise in capillary pressure, but it would be rash to say what fraction of the rise would correspond to a rise in capillary pressure, or that the rise is in all circumstances proportionately the same. Duke-Elder found in general that the rise in intra-ocular pressure in experimental animals was about one-tenth of the rise in arterial pressure, but outside the experimental environment this relationship probably does not hold. It would seem that, teleologically speaking, the vascular system is designed to provide a reasonable constancy of capillary pressure; changes in the calibre of the arterioles may produce changes in the peripheral resistance so that a rise in arterial pressure could be largely compensated and the capillary pressure remain comparatively unchanged.

Recently Bárány (1946—7) has shown that unilateral closure of

the carotid artery in the rabbit causes a fall in intra-ocular pressure associated with a fall in arterial pressure; after a time, however, the intra-ocular pressure returns to normal although the arterial pressure remains permanently depressed in the ear of the operated side. Bárány's results seem to show that the intra-ocular pressure does, indeed, respond to a sudden change in arterial pressure, but that there is some compensatory mechanism at work which eventually keeps the intra-ocular pressure independent of the arterial. Bárány has argued that the response of the eye to a change in arterial pressure is not by any means as large as might be expected on the basis of the dialysis theory if it is assumed that the capillary pressure remains a constant fraction of the arterio-venous difference. This assumption, however, requires justification.

The influence of the colloid osmotic pressure of the plasma on the intra-ocular pressure may, as we have seen, be deduced from the simple equation already stated : a decrease in the former should raise the latter and *vice versa*. In experimental animals these deductions have been borne out qualitatively. Dilution of the plasma with isotonic saline undoubtedly causes in experimental animals a considerable rise in intra-ocular pressure (Duke-Elder, 1931); it is difficult to increase the colloid osmotic pressure of the plasma by injections of gum acacia; Bárány (1947) has recently suggested that the earlier results of Duke-Elder (1931) may have been a factitious result of the toxicity of the gum acacia rather than a true osmotic effect. The decrease in intra-ocular pressure following a massive injection of hypertonic NaCl or sucrose belongs to the same category of osmotic effects; temporarily the osmotic pressure of the blood is raised in comparison with that of the aqueous humour and water is withdrawn from the eye by osmosis. If the high osmotic pressure of the plasma were maintained for some time, as in experimental animals, the extra NaCl or sucrose would diffuse into the eye and so tend to lower the osmotic pressure difference, and eventually the intra-ocular pressure would tend to return to normal. The effects of long-continued maintenance of an abnormal colloid osmotic pressure of the plasma may be observed in man in nephritis : Robertson (1939) has emphasised that there is no coincidental rise in the intra-ocular pressure in this condition and has made this the basis for the claim that the aqueous humour is formed as a pure secretion. His conclusions indicate the existence of some compensatory mechanism whereby slowly developing and long maintained changes in the osmotic pressure of the plasma may be neutralised in so far as the intra-ocular pressure is concerned.

This compensatory mechanism is at present unknown; but we may suppose it may involve two components, one vascular and

the other concerned with drainage of fluid from the eye. The presence of local axon reflexes exerting a powerful influence on the ocular circulation has been demonstrated (Duke-Elder, 1931); the eye is the only organ in the body wherein these have been found and in their presence is surely of significance. Moreover, the presence of a central mechanism (? hypothalamic) maintaining the control of the tonus of the eye at a relatively constant value would merely bring this into line with practically all physiological functions. About this at present we know nothing; but many facts regarding the tension of the eye and the interdependence of the tensions of the two eyes suggest its presence.

VI. *The circulation of the intra-ocular fluid.*—The evidence in favour of a continuous drainage from the eye is largely clinical, depending on the occurrence of iris bombé and the effects of denying access of the fluid to the angle of the anterior chamber. There have been several attempts to measure the rate of drainage or flow in experimental animals. Thus Troncoso (1921) measured the dilution of the blood in the anterior ciliary veins, and, on the assumption that this dilution was due to a bulk reabsorption of aqueous humour, computed that the rate of drainage was about 2 to 3 cu. mm. per min. Friedenwald and Pierce (1932) replaced the aqueous humour with plasma in an attempt to block the drainage route completely; they then measured the rate of inflow into the eye and argued that this was the normal flow. This method is open to some very serious objections, principally owing to the radical disturbance of the difference in colloid osmotic pressure between the two fluids. He obtained a flow-rate of 1 cu. mm. per min. in the dog. Kinsey and Grant (1942) computed a value of 4 cu. mm. per min. in the rabbit from the observed rate of penetration of radioactive sodium but the computation rests on assumptions that have not been proved and are difficult to justify in the light of our present knowledge. There has thus been no definite proof of a bulk *non-selective* drainage from the anterior chamber of experimental animals; but this has been provided recently in our laboratory (Davson, Duke-Elder and Maurice, unpublished). The principle adopted was to replace (under suitably controlled conditions) the aqueous of the cat by an artificial aqueous humour containing about 100 mg. per 100 c.c. of inulin (a large molecular weight substance that could only leave the eye by a non-selective drainage route: diffusion through the blood-aqueous barrier would be out of the question). Throughout the experiment the concentration of inulin was maintained at a higher level in the blood than it was in the artificial aqueous humour; any loss of inulin from the eye must therefore have been due to a bulk-flow mechanism since diffusion through the blood-aqueous barrier (assuming this to have been made sufficiently abnormal by the

experimental technique to permit the passage of inulin) could only occur from blood into the eye. After an interval of fifteen minutes or half an hour the "aqueous humour" was withdrawn and submitted to analysis. The results proved that inulin may be drained away from the eye and represent the first unequivocal proof of drainage in bulk.

It is obvious that the composition of the aqueous humour will be materially altered by this drainage; and it is equally obvious that it will upset any assumptions regarding the height of the intra-ocular pressure based on the formation of the intra-ocular fluid alone. The position is rendered still more complicated by the demonstration of aqueous veins by Ascher (1942—4) supplementing the original conception of drainage through the canal of Schlemm alone. It is interesting that Friedenwald and Pierce (1932) brought forward evidence to show that the capacity of drainage increased five to ten times if the intra-ocular pressure were raised a few mm. Hg above its normal level. Further consideration, both theoretical and experimental, on the influence of capillary and osmotic pressure on this mechanism will certainly produce results of more than usual interest.

## DISCUSSION

From the above short recapitulation of experimental facts it is obvious that the intra-ocular fluid cannot be a simple dialysate in equilibrium with the capillary plasma. It is true that the metabolism of the sugars is largely compatible with such a theory—simple dialysation through the jellyish cement substance occupying the intercellular spaces in the capillary endothelium and epithelial membranes, the watery spaces of which act as pores. A study of nitrogenous substances, however, completely upsets this view-point; urea penetrates more slowly than glucose although it has much the smaller molecule; the same is true for creatinine and more so for amino-acids. Penicillin is smaller than sucrose yet its rate of penetration is very slow indeed, about one fifth of that of sucrose. Evidently the presence of the nitrogen atom in the molecule slows down the rate of penetration, in comparison with a molecule of the same size without nitrogen; this is tantamount to saying that the chemical composition of a substance is more important as a determinant of rate of penetration of the barrier than its molecular size. From this it may be concluded that some substances at least must penetrate by way of the cells; the interstitial spaces could not select molecules on the basis of their structure, such selection being a characteristic of the envelopes of individual cells. A striking instance of the importance of chemical structure in penetration is shown by the observation of

Palm (1947) that ethyl alcohol penetrates very rapidly into the aqueous humour, some five to six times as fast as glucose; undoubtedly this is because of the high fat solubility of ethyl alcohol which permits it to diffuse rapidly through cellular membranes. Moreover, the excess of electrolytes with the consequent excess of osmotic pressure of the intra-ocular fluid suggests that some cellular activity is in question. Studies of the most varied nature in other organs of the body have consistently failed to produce any evidence that the capillary wall acts otherwise than as a simple filter; it may block substances, but it has not, so far, been detected in the act of secreting any substance (Landis, 1946). The presumption is, therefore, than any cellular activity is localised in the lining epithelium of the eye (presumably mainly in the ciliary region).

The second general point which emerges is that not only is the mechanism more complicated than dialysis since it differentiates between substances on a chemical basis, but the blood-aqueous barrier differs radically in different localities of the globe. In general, when a given substance penetrates into the aqueous humour it also penetrates the vitreous body more slowly. We have seen that in the most simple case—that of sugars—entrance into the anterior chamber (through the iris) is easy and undifferentiated except in respect to the physical size of the molecules: entrance into the vitreous, on the other hand, is slower and shows some chemical discrimination. By freezing the eye suddenly during the diffusion process it may be shown that certain substances enter the vitreous body predominantly by way of the ciliary body and diffuse backwards towards the posterior pole; other substances, however, can apparently enter the vitreous body rapidly from all parts of its periphery (Davson and Duke-Elder, 1948; Davson, Duke-Elder, Maurice, Ross and Woodin, in press). Sodium and potassium are two instances of substances the route of which to the vitreous body is largely confined to penetration from the ciliary region; glucose and thiocyanate, on the other hand, are examples of substances that can diffuse from the choroidal and retinal circulations. This is a remarkable finding and brings out the strong analogy, if not the identity, between the capillaries of the cerebral and retinal vascular systems. It has been recognised for some time that the capillaries of the cerebral system are radically different from those in other parts of the body. Palm (1947) has recently shown that, alone of the capillaries of the body, those of the central nervous system and the retina do not take up certain acid dyes (trypan blue). On the other hand, Friedenwald and Stiehler (1938) found that acid dyes penetrated the ciliary capillaries with ease. In the rest of the body the

capillaries show no power of differentiating between such substances as urea and sugar and it is generally accepted that diffusion through the walls of these capillaries is a matter of diffusion through quite large intercellular spaces, spaces that are large enough to allow the molecule of inulin, for example, to pass through. The capillaries of the cerebral system, on the other hand, seem to allow sugar and various monovalent ions to penetrate into their surrounding interstitial or perivascular spaces at much slower rates, and they also show some selectivity. If the retinal vessels were similar to those in the muscles, for example, we should expect glucose, sucrose, raffinose and even inulin to penetrate rapidly into the vitreous body, and the fact that penetration of these substances, when it does occur, is less rapid than that into the aqueous humour indicates the highly selective character of the retinal capillaries. The vitreous body, of course, comes into relation with the capillaries of the uveal system—the capillaries of the choroid and ciliary body; here, however, it is separated by membranes and cellular structures from these capillaries and their interstitial fluid (the epithelium of the ciliary body and the whole of the retina including the pigment epithelium). It might be presumed that these structures could impart some selectivity to this part of the barrier separating the vitreous body from the uveal blood plasma.

Although the simple dialysis theory appears to be wrong, as the most recent work from our laboratory (among others) has shown, nevertheless the fairly close similarities in chemical composition of aqueous humour and plasma, together with the partial conformity of the intra-ocular pressure to changes of osmotic pressure and capillary pressure indicate that the simple physical factors of diffusion and osmosis are operative. Can these apparently contradictory findings be reconciled? At the moment there seem to us to be two general possibilities. First we may consider in detail an idea adumbrated from this laboratory ten years ago (Duke-Elder, 1938); on this basis the aqueous humour is formed primarily as an ultra-filtrate of plasma and, superimposed on this simple process, there is some activity which modifies the concentrations of certain substances, notably sodium and chloride, in the aqueous humour, giving certain peculiarities including an excess of osmotic pressure to this fluid. It is well recognised that the permeability of membranes is influenced by differences in the surface electrical charges and in the hydrophilic swelling of the proteins on either side of the membrane so that some degree of uni-directional permeability and the capacity for maintaining concentration gradients exist. Such a complex membrane offers itself in the ciliary epithelium, and the work of Friedenwald and Stiehler (1938) suggests a possible mechanism. They suppose that the energy

necessary for such modifications depends upon a difference of potential maintained between the ciliary stroma and epithelium by oxidative and reductive processes owing to the presence of Warburg's respiratory enzyme in the latter. It is true that these conclusions are based on the intra-vital action of dyes—a very confused and difficult problem susceptible to several explanations: but the possibility of some such activity cannot be ruled out of court. Further exploration along these lines would be of great interest.

If we assume such an activity on the part of the ciliary epithelium, as a result of this excess of pressure the driving pressure of fluid into the eye consists of the whole of the capillary pressure (instead of the capillary pressure *minus* the colloid osmotic pressure of the plasma) *plus* an excess of osmotic pressure. Fluid is thus forced into the cavities of the eye with an available pressure-head of from 50 to 75 mm. Hg. Since there is no counter-pressure the intra-ocular pressure must equal this driving pressure unless there is a leakage of fluid out of the eye; the intra-ocular pressure is in effect 25 mm. Hg so that there must, in this view, be a rapid drainage of fluid out of the eye. This outflow would therefore be of maximal importance in the mechanics of the ocular tension, and blockage of the drainage routes must, on this basis, result in a serious rise in intra-ocular pressure since the normal intra-ocular pressure is maintained at its low level only as a result of leakage.

An alternative theory that must also be borne in mind when considering the experimental data is the following:— The aqueous humour may be elaborated entirely within the cells of the ciliary epithelium and possibly to a less degree in other cellular linings of the eye. The fluid so formed is extruded into the posterior chamber of the eye as a "primary aqueous humour"; as a pure secretion it may have characteristics entirely different from those of the blood. The fluid so formed would be forced into the posterior chamber with a certain secretion pressure; if drainage occurred at the angle of the anterior chamber this forcing of fluid into the eye would result in a flow through the pupil. The primary aqueous humour on its passage out of the eye would not, however, be insulated from the blood plasma, but would be in communication with it through the iris and, through the medium of tissue-fluid, through the intercellular spaces of all the lining membranes; it would thus tend to attain diffusion equilibrium with the blood. If diffusion equilibrium were completely attained the result would be that the aqueous humour would appear to be a simple dialysate in spite of its secretory origin. It can be postulated, however, that the aqueous humour does not remain in the eye long enough for

this diffusion equilibrium to be established, so that an intermediate state is achieved in which it has strong characteristics of a dialysate but betrays its secretory origin in important details, such as an osmotic pressure greater than that of the plasma, a higher concentration of sodium and chloride than required of a dialysate, a low concentration of urea, a high concentration of ascorbic acid, and so on. On the basis of this theory most substances must enter the eye by a cellular route whereas on the modified dialysis theory discussed above, much of the fluid formation could have been by way of the intercellular spaces only, the osmotic excess of material being added by the cellular activity of the lining membrane. On the experimental evidence, however, this hypothesis would seem unlikely.

Such are two tentative suggestions. Others may offer themselves, but it is obvious that in the present state of factual knowledge no pragmatic conclusion can be reached. The problems presented are full of interest and are not without their difficulties; their solution must await the results of more extensive and detailed experimental work.

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# PARTICIPATION OF THE OCULAR APPENDAGES IN SYMPATHETIC OPHTHALMIA AND ITS *BEARING ON ENUCLEATION*

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THE special incentive for this paper is my conviction that not infrequently following the enucleation of the exciting eye in sympathetic ophthalmia a considerable amount of inflamed tissue is left in the orbit. Sufficient emphasis does not seem to be placed on the fact that although sympathetic ophthalmia is primarily a disease of the inner eye yet the appendages may also be involved simultaneously.

## NATURE OF SYMPATHETIC OPHTHALMIA

Histologically sympathetic ophthalmia declares itself in the guise of an infiltration of lymphocytes, epitheliod cells and giant cells in the uveal tract of each eye. The peculiarity lies not so much in the elements of the infiltration, which are similar to those of tuberculosis, but rather in the selective affinity that the disease exhibits for uveal tissue. A characteristic feature of the disease is the tendency of the infiltration to expand outward beyond the globe. Inwardly, any involvement of the pigment epithelium and retina is invariably so slight as to be of no real consequence. Nor is the choriocapillaris attacked, apparently because the interspaces between the capillaries is composed of tissue that is not typically uveal and therefore is not suitable soil.

## CAUSE OF SYMPATHETIC OPHTHALMIA

As far back as 1905 Parsons, in his Pathology of the Eye, expressed his opinion that sympathetic ophthalmia " is an endogenous infection by ultravisible organisms." The accumulated evidence of countless histological examinations of the exciting eye has served to strengthen this theory. Certainly the inflammatory reaction of the tissues attacked presents all the earmarks of a non-pyogenic infection. The most mysterious aspect of the disease is the fact that the virus supposed to be responsible has never been isolated or seen. In any event, the very essence of sympathetic ophthalmia is a perforating wound in one globe through which the virus may enter.

## PATHWAYS OF THE VIRUS AS REVEALED BY INFLAMMATORY REACTION (OMMITTING MANY MINUTIAE)

A. *Pathway along the uveal tract.* Perforations in the region of the ciliary body, which, to borrow a term from Nettleship, is called " the dangerous zone," are the most feared because they are apt to be accompanied by prolapse of the iris and ciliary body, either one of which forms a favourable point from which the virus may travel into the interior of the eye. When the opening is large, the blood supply to the prolapse being little impaired and the part being released from intra-ocular pressure, the reaction may be so great as to attain tumour-like proportions and resemble a staphyloma (Fig. 1). On the other hand, there may be little or no reaction at or near the opening, for with the globe as with any other part of the body, it is possible for bacteria to enter without causing a primary lesion. The advance of the virus posteriorly may be blocked completely by a zone chorioretinitis produced by traction on the part of a detached retina. Such confinement of the infiltration to the area near the perforation is a most striking anatomical proof of the extra-ocular origin of the virus (Fig. 2).

The development of the infection in the choroid may be divided into two stages. (1) The appearance of small lymphocytic foci in and around the walls of the larger veins. (2) The complete replacement of the vascular layer by the specific infiltration. All of these changes, as a rule, are more advanced in the iris and ciliary body—another point in favour of the theory that the virus enters through the wound.

The infiltration is to be found in its purest and heaviest form in the circumpapillary and macular regions of the choroid. Here the least damage is done at the time of the perforation and here the layer is the thickest and the blood supply the richest.

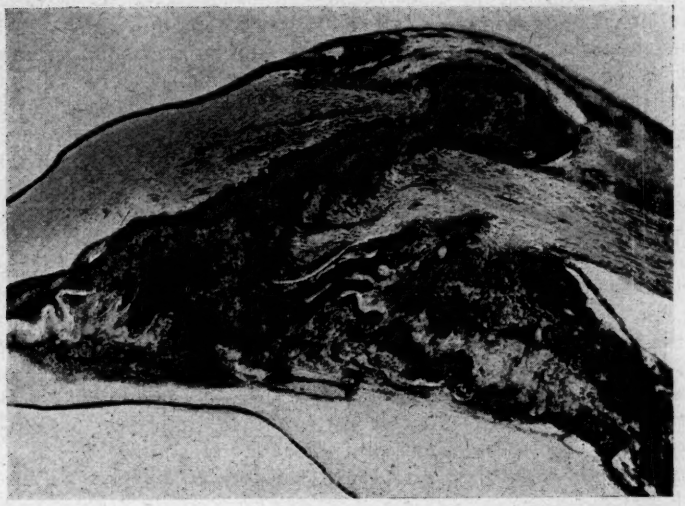

FIG. 1.

Tumour-like extra-ocular nodule of specific infiltration replacing prolapsed iris and simulating staphyloma.

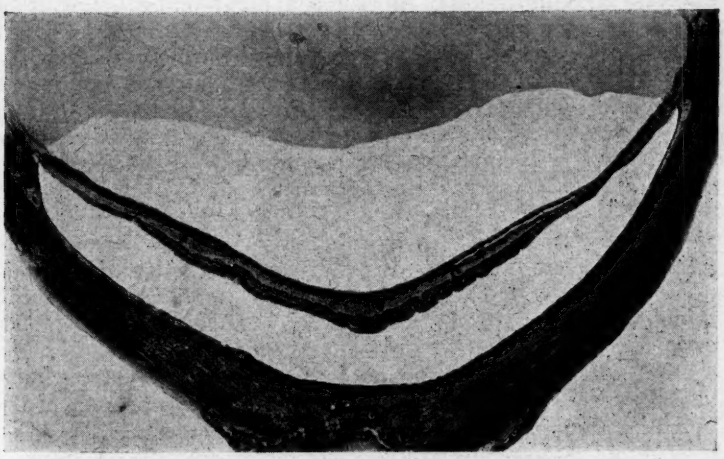

FIG. 2.

On either side a large dense nodule marks the point at which the retina becomes detached and the specific infiltration ends.

B. *Pathway of the virus through the globe into the tissues of the orbit.* The virus, judging always by the presence of the infiltration, leaves the inner eye by the same routes as those chosen by the cells of a malignant melanoma of the choroid. It may infiltrate layer after layer of the sclera and at the same time pass through the preformed emissaria. Anteriorly, the root of the iris is a favourite site for the accumulation of the specific cells, thereby clogging the angle and accounting for secondary glaucoma. The pectinate ligament may be destroyed and files of lymphocytes may replace the tissue between the internal and external sulci, leading to the sympathetic staphyloma seen in the worst cases. Rarely nodules occupy Schlemm's canal. Posteriorly, the segment of the sclera facing the muscle funnel is pierced by numerous large emissaria for the passage of the short ciliary arteries and nerves. This part of the sclera may be considered as the dangerous zone for the egress of the virus just as the ciliary region is the dangerous zone for its ingress. The heavy choroidal infiltration passes by continuity into the lamina fusca of the sclera and replaces it. In sympathetic ophthalmia, as in malignant melanoma, every emissarium is a *locus minoris resistentiae.* The infiltration passes without hindrance through these openings to the episclera and the space of Tenon. The destruction of the outer layers of the sclera proceeds with that of the inner layers. At the same time the middle layers may be permeated with nodules. At the height of the infection the implication of the sclera, through and through, is an outstanding feature of sympathetic ophthalmia. The infected sclera may be thought of as fairly reeking with the virus (Fig. 3).

By the union of the parts the virus passes into the insertion of the inferior oblique muscle. Sympathetic nodules have been reported replacing muscle bundles as far as 10 mm. from the sclera. Foci of lymphocytes are not uncommonly seen scattered in the fat that fills out the muscle funnel.

C. *Pathway of the virus into the optic nerve.* The infiltration in the choroid presses through the emissaria that surround the scleral canal into the sulcus of the intervaginal space of the optic nerve where a large number of cells may accumulate. On the way through the sclera the circle of Zinn may be enmeshed. Lymphocytic foci develop particularly along the pial sheath (Fig. 4). There is thus set up a sympathetic leptomeningitis of the intervaginal space. The infection is transmitted into the stem of the nerve by the pial sheath and the septal system derived from it. very rarely a typical nodule may be found some 12 mm. back of the lamina cribrosa. It is important to state here that the sheaths of the optic nerve are involved only in far advanced cases. The choroidal infiltration may make its way forward around the

FIG. 3.

The outer and inner layers of the sclera in the posterior quadrant are undergoing destruction. Lymphocytic foci are scattered in the middle layers. The overlying choroid shows an infiltration of lymphocytes, epitheliod cells and giant cells in its purest form. Similar elements have replaced the external layers of the sclera.

FIG. 4.

Files of lymphocytes infiltrate and separate the layers of the pial sheath. Note that infiltration extended beyond the point of excision.

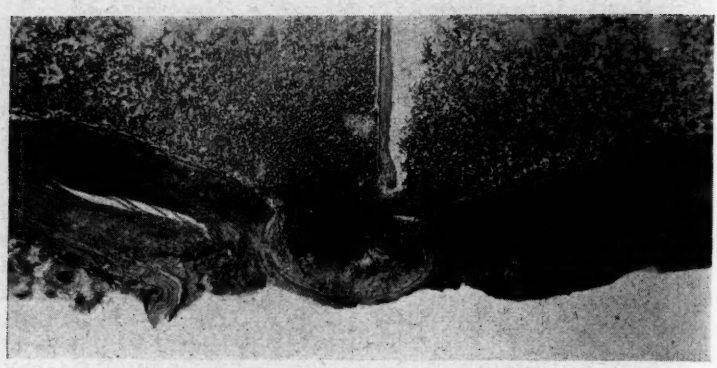

FIG. 5.

The optic nerve was excised within the scleral canal no doubt leaving much infected material behind. Small lymphocytic foci can be made out in the fat to the left.

opening in the lamina vitrea and appear as a collar surrounding the papilla. It is certain that the infection is not transferred to the other eye through the optic nerve and chiasm because the opposite nerve never shows signs of ascending inflammation.

## ENUCLEATION OF THE EXCITING EYE

McKenzie, who in 1835 wrote the first scientific description of sympathetic ophthalmia, seems to have made no suggestion as to its prevention, although he prescribed a number of palliative remedies. It remained for Prichard, in 1851, to advise the excision of the injured eye, but only after the fellow eye began to show signs of inflammation. In a few cases, probably those in the prodromal stage, the removal of the offending eye did arrest the process in the uninjured eye, thus adding further proof to the sympathetic nature of this disease. In most cases the condition continued to grow worse and in a few it seemed to be actually aggravated by the excision of the injured eye so that there grew to be considerable opposition to the operation.

Later, the crowning surgical step was made by Critchett, who advised the removal of the injured eye before there are any signs whatsoever of iridocyclitis in the other. In the active stage of any form of iritis Critchett took a strong stand against any attempt to perform an iridectomy, an operation which had been greatly overestimated as a cure for all kinds of iritis. It is the universal practice to-day to excise at once every globe which after a perforation shows

retraction of the wound, hypotony, sensitiveness either spontaneously or to light touch, and failing vision.

The object now is to apply with discretion the histological facts to the procedures for the removal of the exciting eye. Whenever enucleation is performed as a preventive measure the ordinary method of cutting the nerve on a level with the outer surface of the sclera may be employed with safety. Once signs of sympathetic ophthalmia appear the only hope of saving the uninjured eye lies in the immediate removal of the source from whence came the invasion and from which fresh virus would constantly be sent forth. Before operating it is possible to gain valuable information from examination of the sympathising eye as to the state of the infiltration in the injured eye and its appendages. If central synechia of the iris can be partially broken up and kept under control it is likely that the infiltration is in the first stage in the injured eye or at least is still intra-ocular. Should the iris be swollen and discoloured or, most important of all, should the pupillary zone be hopelessly bound down, these are signs that the inflammation has reached its acme in the exciting eye and that the extra-ocular structures are infected. The difficulty of removing an acutely irritated and painful globe surrounded by orbital cellulitis seems to account for the many instances in sympathetic ophthalmia in which the optic nerve is cut within the scleral canal. A long strip of the inferior oblique muscle should be excised and the optic nerve and the retrobulbar tissues around it should be removed almost to the apex of the muscle funnel. The wound should be left open to drain. If there remain in the exciting eye some degree of vision it is axiomatic to postpone enucleation as the benefit of the operation is always problematical and there is no justification for sacrificing even the faintest vision.

## LINDAU'S DISEASE—PROGRESSION IN AFFECTED FAMILY

BY

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IT is unfortunate that Lindau's disease has been inextricably associated with allied conditions in so many published reports of the clinical findings and pathological records. It is a rare condition, and to substantiate the diagnosis it seems reasonable to require that the presence of multiple haemangioendothelioma be verified, for at

least one member, with a similar tumour in another member of the family. It seems certain that this will happen more frequently during the life of the patient, as the advances made in surgery of the brain indicate that earlier diagnosis is probable.

We have had the opportunity to follow the course of Lindau's disease in a family where three of the four members of a sibship has each undergone the successful removal of cerebellar tumours, which on pathological examination proved to be haemangioendothelioma.

The death of sibling two, a female, occurred 3½ years after the cerebellar tumour was removed from sibling four, the youngest and only male in the family. All four members have had eye involvement, and sibling two had a cataract, in a glaucomatous eye which after extraction of the cataract developed pain so severe that enucleation resulted. The early pathological report showed that a retinal detachment due to intra-ocular haemorrhage was present, and it was only after sibling one had a cerebellar tumour removed and verified as a haemangioendothelioma that a further search was made for the presence of a tumour in the enucleated eye of sibling two. A haemangioendothelioma was found when further sections were made and the findings reported in the Transactions of the American Ophthalmological Society, Vol. 37, 236-250, 1939, and Archives of Ophthalmology 23: 564-576, 1940. The interest in this remarkable family, which produced for several years three verified living cases of Lindau's disease, may justify the following brief review of the present status of the various members and the clinical report of sibling IV who previously was reported as being healthy.

## REVIEW

In 1912 the mother of this family, at the age of 22 years, had a painful eye enucleated, according to Dr. Wilber Fraser of Ottawa who found the record in Dr. Minnes' files. The globe was opened and a complete cup-like calcification of the choroid was found, but no microscopic sections were made. The family state that her death resulted after an operation for a brain tumour in 1918, but no record of this could be found at the hospital in Ottawa.

*Sibling II*: In 1934, while bending over, suddenly lost the sight of her left eye, due to an intra-ocular haemorrhage. On February 24, 1936, at the age of 23 years, at a second stage cerebellar exposure a vascular tumour the size of a walnut, which pressed on the medulla, was found in the lower hemisphere. The upper part of the spinal cord was cystic.

Roentgen therapy was administered to the region, seventeen

*PLATE I.*

Fundus O.D. of Sibling I before radon treatment ; showing detachment about peripheral tumour and dilated vessels.

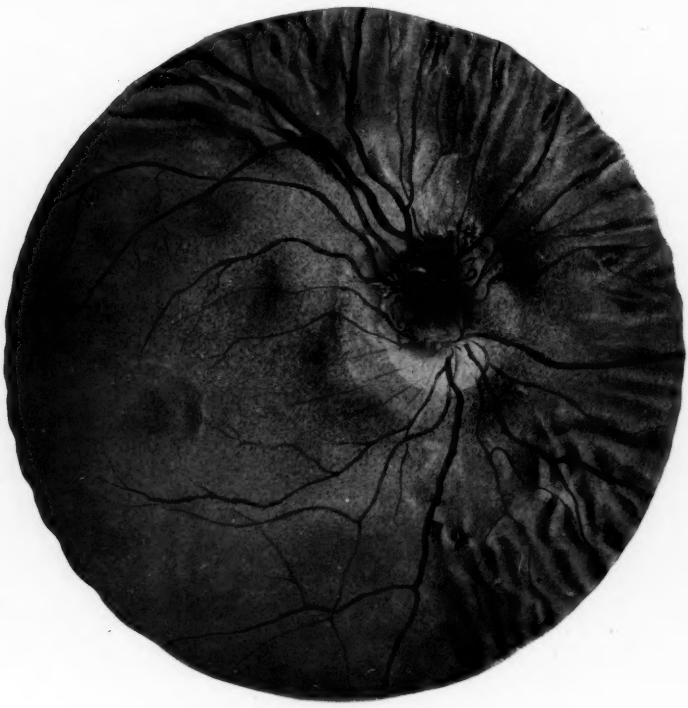

PLATE II.

Fundus O.D. of Sibling IV before radiation. The capillary angiom covers the upper part of the disc and extends into the retina above.

times, and she was re-admitted for vomiting caused by this treatment.

March 30, 1937: Left cataract extraction.

May 31, 1937: Enucleation L.E. blind and painful due to secondary glaucoma. The pathological report of this eye at first showed that the detachment of the retina was due to intra-ocular haemorrhage. A re-examination was made in April, 1939, and a haemangioendothelioma was found and reported.

August 10, 1939: A cystic cerebellar haemangioendothelioma was removed and verified by pathological examination. Following this she remained well and carried on her work as a nurse until headaches and unsteadiness of gait developed early in 1947.

August 5, 1947: At a re-exploration of the cerebellum two large tumours were found; one was the size of a hen's egg, the smaller in the roof of the fourth ventricle. Both were removed, and it was found that the tumour infiltrated the muscles of the neck.

August 8, 1947: Following the operation she developed signs of medullary failure, was unable to swallow, and died. The autopsy revealed multiple cysts of the pancreas, kidneys, chronic interstital pancreatitis and terminal broncho-pneumonia.

*Sibling I*: Female, aged 29 years.

May 6, 1938: A haemangioendothelioma, verified by pathological examination, was removed from the left cerebellum. This firm tumour was the size of a walnut. It was attached to the dura, lateral sinus and tentorium by large thin-walled vessels, which contained arterio-venous blood. For three years she had noticed a loss of vision in the right eye. The fundus showed central degenerative changes and her visual field showed a lower nasal defect which extended to 40 degrees from central fixation. With a widely dilated pupil, a whitish mass with a haemorrhage on its surface was seen well out to the periphery. The upper temporal vessels were greatly dilated (see plate I).

May 28, 1939: Four radon seeds of 0·7 millicuries each were placed subconjunctivally on the sclera, opposite the site of the tumour and removed seven days later. The seeds were tied separately to a silk thread and this part of the suture was dipped in thin pyroxylin solution. Moderate reaction followed at first, but for many months a depression at the treated area remained on the globe. Possibly one-half the dosage would have been sufficient to destroy the retinal tumour.

March 30, 1942: She complained of staggering, weakness of left arm and difficulty in controlling her speech. At this time RV=Cf. at 2 m and LV=6/18. The right eye was divergent 40 degrees.

April 24, 1947: A tumour the size of a walnut was removed from approximately the same area as at the previous operation. Dr. Eric

Linell reported the tissue as being extremely cellular. The cells were uniform in size with fusiform nuclei and a moderate amount of cytoplasm. The cell boundaries were indistinct. Some large blood channels were present but the Mallory stain showed capillary-like channels in large numbers. No mitotic figures could be seen with the cresyl violet stain.

August 6, 1947: The family stated that she still complained of unsteadiness of gait and deafness in the left ear, but she was able to do her housework.

*Sibling III*: A female, was re-examined on August 6, 1947. The naevus on the limbus of the left eye was less distinct than when seen in 1938. She looked well and stated that her health had been good.

*Sibling IV*: A synopsis of his voluminous history follows: Flt. Sgt. W. R., a white male, aged 27 years, began to complain of headaches, which were worse when he was in the prone position and during the morning. They were severe and gradually became worse. In July, 1942, he overturned a plane while landing it, and a careful physical examination followed. His history was referred for advice to Dr. K. G. McKenzie, who recalled the family history and asked for his admission to Christie Street Military Hospital, as from the record the presence of a brain tumour was considered possible.

January 28, 1943: The vision in each eye was normal with correction. The fields of vision showed only a slight enlargement of the blind spot in the right eye and the fundi were reported as being normal, but one week later it was stated that the right disc showed blurring on the upper and nasal borders with a moderate physiological cup. The left disc showed a slight haze at the upper border. Horizontal nystagmus was present, bilateral, more marked on looking at the right. The gag reflex was absent, the electrocardiograph negative. The impression was that the relative hypertension 154/114, nystagmus and absent gag reflex might be due to hyperinsulinism, an adrenal or intracerebral tumour.

February 2, 1943: Dr. McKenzie, in view of the above examination, combined with the family history, injected the ventricles and found the left lateral hemisphere under pressure, the whole ventricular system was enlarged and the picture suggested the presence of cerebellar angioma. He was transferred to the Toronto General Hospital for the operation.

February 27, 1943: A vascular tumour the size of a walnut was found in the angle between the right tonsil and the cerebellar hemisphere which shelled out by finger dissection. See Figs. 1 and 2. The post-operative treatment required a re-opening of the wound to remove an extra-dural blood-clot that developed within

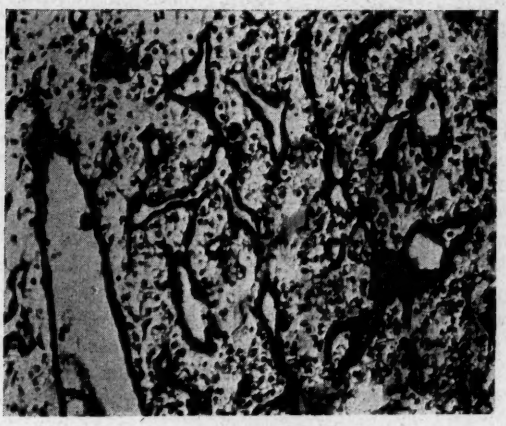

FIG. 1.—SIBLING IV.

Medium power ×120. Mallory connective tissue stain showing many vessels with fibrous walls, the intervening spaces being filled with endothelial cells.

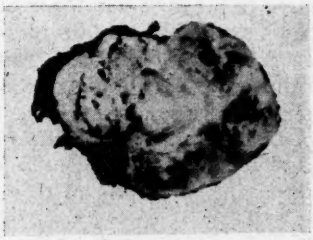

FIG. 2.—SIBLING IV.

Bisected tumour, 35×30×15 mm. showing fibrous structure and cystic degeneration.

24 hours, but by March 5, 1943, he was well enough to be transferred to his military hospital. At this time he had a marked horizontal nystagmus, dizziness and bilateral 6th nerve paralysis with right sided inco-ordination, but five days later he was able to sit up. One week later he could walk with help.

April 7, 1943: No headache and no diplopia was present, but there was slight inco-ordination of both hands and feet. He was discharged to return for a check-up visit in six months.

April 9, 1947: He was re-admitted to Christie Street Hospital

complaining of fatiguibility, dysfunction of balance and slight loss of hearing of the right ear.

Laboratory examination.—Sedimentation rate 16 mm. urine acid, specific gravity 1021, negative for albumin and sugar, Kahn negative. Examination revealed no corneal reflex and cranial nerves essentially negative. Personal history: He had returned to work two months after his operation, as a checker in a lumber camp, but at the time of this admission he had been teaching in a school.

February 2, 1947: The fields of vision showed slight enlargement of the right blind spot. The pupils were equal in size, reacted to light and convergence, full ocular movements were present with no nystagmus. The disk of the right eye showed a reddish elevation over the upper half with new blood vessels. The superior temporal vein was engorged. Radiation was suggested for this developing angioma. He was seen also at this time by Dr. McKenzie, who found no evidence of a recurrence of the brain tumour.

June 10, 1947: See colour drawings of the right fundus showing angioma.

August 15, 1947: R.V. 6/12-1. L.V. 6/9-2.

In the fundus of the right eye the media were clear. There was considerable connective tissue over the upper part of the disk with new loops of capillaries extending up into the retina. These were elevated about three dioptres. The mass was purplish-red and extended down over the cup. The fundus of the left eye essentially negative, only a slight crescent and clear, physiological cup. Partly on account of his obligation to teach in September and his good vision, he requested that the treatment be delayed. He stated that his four children: girl of 8, boy of 6, girl of 2 and a one-month old boy were well.

January 10, 1948: Fourteen treatments have been given to the area of the developing eye tumour. The vision R.V.=6/18, L.V.=6/12 and normal in each eye with correction.

The right fundus showed an area of grey oedema over the tumour mass which was seen with a plus four lens. Above the disk the capillary loops extended higher into the retina when compared with the drawings made in May, 1947.

## DISCUSSION

The familial condition where multiple capillary haemangioendothelioma occur in the cerebellum, cerebrum, retina, spinal cord, kidneys, pancreas, epididymis, liver and bone, with occasionally hypernephroma, should be termed Lindau's disease.

A review of a family and the most recent case history in the only male has shown that the cerebellar tumour was verified for sibling I at the age of 29 years by pathological section and an eye tumour was treated by radon seeds. Sibling II—the cerebellar tumour was verified at operation at the age of 23 years and by pathological section at two subsequent operations. The eye tumour presented a similar pathological appearance. Sibling III had a naevus of the limbus of the left eye, which became less apparent after nine years. Sibling IV: The new case was verified by pathological examination at the age of 28 years and after extensive radiation an eye tumour, capillary in type, has slightly progressed in four years.

*Acknowledgment:* To Dr. K. G. McKenzie, my thanks and congratulations for the surgical care and remarkable results that have meant so much to the members of this family. Dr. Eric Linell was responsible for the excellent pathological reports and photographs. Miss Wishart made coloured drawings, which add much to the written description. Also thanks to the Departments of Surgery, Neuro-Pathology, Veterans' Affairs, Ophthalmology, Art and Photography.

## METHODS OF INVESTIGATING EYE MOVEMENTS

BY

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OPINIONS differ widely at the present time with regard to the ability of a subject to perform accurate fixation, for whereas some hold that the eye is constantly making rapid oscillations, on the presence of which visual acuity for fine detail actually depends, others hold, on the contrary, that such oscillations are absent in normal subjects and that if these movements were present, far from aiding the perception of detail, they would have the effect of seriously interfering with it. Thus Hering (1899) thought that the irregularities at the contours between the images of objects which are produced by the retinal mosaic are smoothed by chance eye movements. Anderson & Weymouth (1923), Averill & Weymouth (1925), and Marshall & Talbot (1942) have held similar views, and they have extended the consideration to the cases of small differences of size and small defects in alignment. Wright (1942) claims that the eyes are continually performing " twittering " movements, and that in consequence the receptors are able to scan the retinal image in the same way that the bright spot in the cathode ray tube of a television receiver scans the fluorescent screen. He writes, " It is the dimensions of the cones rather than their number

which is the essential factor in determining the visual acuity." Thus a sparse population will perform as well as or even better than a dense one. Adler & Fliegelman (1934), as the result of recording the reflection of a beam of light from a galvanometer mirror which had been attached by surface tension to the sclera of a subject, claimed to have demonstrated the presence of fine oscillatory rotations of the eyeball. Lastly Lord & Wright (1948) have stated that they find evidence which confirms that of Adler and Fliegelman, because their records show that the subject's eye is oscillating with an amplitude of about thirty minutes of arc.

In contradistinction to these views experiments were performed by Hartridge (1947) which were based on the employment of very precise fixation. Thus the position of the fixation points for rays of different colour at the fovea appeared to be identifiable within a fraction of a cone unit, and as a rule ophthalmologists do not find that eye movements interfere with observations of the anterior eye structures by means of the slit-lamp, in which magnifications of between fifteen and thirty diameters are normally employed.

## SECTION 2: PROBLEMS CONNECTED WITH THE OBSERVATION OF EYE MOVEMENTS

A number of different methods have been employed in the past for investigating the movements of the eye. It is not proposed to consider these in detail in this paper, but instead to concentrate attention on optical methods alone, since in the opinion of the authors these are more likely to lead to accurate results than are methods which depend on other principles.

Three main problems have to be faced in designing a satisfactory technique.

(*a*) Obtaining the necessary accuracy.

(*b*) The elimination of chance movements of the head.

(*c*) Eliminating the effects of the heart beat.

With regard to the first problem the precision needed corresponds to a rotation of the eyeball of one minute of arc. This is the minimum precision which should be aimed at. If a method could be devised which provided a precision of one-tenth of this, that is six seconds of arc, it would be advantageous because one cone unit, namely 2 mm. at 10 metres, the standard proposed by one of us elsewhere (1947), corresponds to an angle of 41·236 minutes of arc, and it would be an advantage therefore to be able to express the rotation of the eye in terms of cone units and fractions of a cone unit. If a human eye rotated through an angle of one minute of arc the various parts forming the coats of the

eye would suffer a rotatory displacement of about 2·4$\mu$. The optical method therefore has to satisfy the requirement of being able to provide measurement of such a displacement to at least an accuracy of 2·4$\mu$, and if possible to an accuracy of 0·24$\mu$.

With regard to chance head movements these are frequently quite large. The precise cause of them is not known. It may be that they are due merely to irregularity in the contraction of the muscles which support the head on the body, and to similar irregularity in the muscles which maintain the position of the body. Another possibility is that the proprioceptive control of the head in relation to the environment lacks high precision. Whatever the cause may be there is little doubt that the head is constantly performing small nodding movements, both lateral and anteroposterial. These are largely counterbalanced by compensatory rotations of the eyeball which, in spite of head rotations, maintain the gaze on external objects. The study of eye rotations during the rotation of a subject, by means of a cinema camera mounted on the same turntable as himself, had already provided us with much information with regard to these compensatory rotations of the eye, but there is little doubt that much remains to be learnt concerning them.

With regard to the effects of the heart beat the eye itself appears to be so arranged in the orbit as to be immune, or almost immune, from the effects produced by variations in blood flow during the various phases of the cardiac cycle. The effects of the heart beat most strongly assert themselves either when apparatus is mounted on the head, attached to a plaster hat, or when attempts are made to immobilise the head by means of pads or clamps externally applied. Because of these circulatory effects in the soft tissues of the head it would appear to be a matter of considerable difficulty to immobilise the head completely. It will be recollected that even the teeth are not in solid contact with the bones of the upper and lower jaws, but that they are inserted into soft tissues which are themselves supplied with blood and therefore pulsating to some extent with the heart beat.

## SECTION 3: THE CHOICE OF SUITABLE EYE STRUCTURE

It is obvious that theoretically any structure accessible to light may be utilised for recording optically the rotations of the eyeball. It is therefore largely the practical considerations which decide what structure provides advantages over others. It is not possible to contrast all the possible structures which are available. A few of the more important only will be considered in this paper.

*The cornea.*—This structure has two advantages. It is readily

accessible and its anterior surface reflects light in the same way that a convex mirror of short radius of curvature reflects light. It was for these reasons that at the suggestion of one of us Vernon made use of the reflection from the cornea, when studying the eye movements which occur during reading.

The corneal reflection has one disadvantage, namely that the movement of the reflected image of the light source is not as great as the actual movement of the anterior surface of the cornea itself, but is about half the movement. In order therefore to measure the rotations of the eye with a precision of one minute of arc it would be necessary to be able to measure the movement of the corneal reflection with a precision of about 1·8$\mu$. There is another disadvantage in using the corneal reflection, namely that deflections may take place owing to alterations in the local thickness of the lachrymal fluid. This is very likely to occur if the reflected image is taken off the eyeball near the margin of either the upper or the lower lid, or if any factor connected with the observations is causing lacrymation.

*The iris.*—This structure in subjects whose irises are not deeply pigmented provides an admirable object for photography, the obvious disadvantage attending its use being the constant alterations in the diameter of the pupil which are all the time taking place in normal subjects. These difficulties may in large measure be avoided by paralysing the iris, either in its dilated condition by means of atropine or in its contracted condition by means of eserine. The line of demarcation between the edge of the iris and the pupillary aperture under either of these treatments provides a sharp edge by means of which the necessary precision should be obtainable. There is one disadvantage however, that it is not easy to illuminate the substance of the iris brightly without at the same time flooding the eye with light. To some extent this difficulty can be offset by directing the illuminating beam towards the subject's blind spot.

*The sclera.*—The sclera may be utilised under three conditions.

(*a*) Where the scleral vessels are partially engorged with blood, so that they provide the necessary landmarks for photography.

(*b*) Where a suitable part of the sclera has been tattooed.

(*c*) Where a suitable foreign body has been placed in contact with the sclera.

Adler and Fliegelman applied a plane mirror to the sclera allowing it to adhere by surface tension. The disadvantage of this technique was that rocking of the mirror could take place owing to the fact that the sclera was curved but the mirror flat. One method of overcoming this difficulty would be to employ a concave lens, the concavity having the same radius of curvature as that

of the sclera, the other side of the lens being polished flat or to a suitable curvature and made reflecting by means of aluminium, silver or rhodium. Such a lens-mirror should not be found to rock during the rotations of the eye. Another method has recently been used by Barlow, namely to apply small drops of mercury to the sclera, and to use these as landmarks. The only difficulty which is likely to be met with here is that the mercury droplets may be slowly swept along in the lacrymal fluid which is emerging under the border of the upper lid and is flowing towards the inner canthus of the eye.

*The retina.*—The retina would appear to have obvious advantages over all the structures which have been previously mentioned, owing to two factors; (*a*) it is the structure which is vitally concerned with movement because it is the movement of the image of the lens system relative to the retina with which we are concerned when studying eye movements, and (*b*) due to the fact that the retina rotates in one direction, when the lens system is rotated in the opposite direction, the apparent movement is double that obtained when making observations on the superficial eye structures which have been mentioned above. The difficulties likely to be met with in practice are those connected with the illumination of the retina, and in the provision of a sufficiently fast film for adequately recording the somewhat feeble light which re-emerges through the pupillary aperture. By choosing a subject with slight retinal pigmentation and by directing the illuminating beam at the blind spot, which is as a rule paler than the rest of the retina, it should be possible to obtain sufficient illumination without at all seriously disturbing the retina and preventing adequate fixation.

*The contact glass.*—It is obvious that if a contact glass could be fitted to the subject's eye, so well-fitting that it moved precisely with even the smallest rotations of the eye, and not at the same time causing painful sensations, it would go a long way to providing the solution of many of the problems indicated in earlier parts of this section, thus the artificial cornea could be given a curve of a much smaller radius than the real cornea, the consequence of which would be that the ray reflected from its surface would undergo a bigger movement for a bigger rotation of the eye than the subject's real cornea. A long-sighted subject is preferable for such a method, because in order to correct his long sight a contact lens with a more highly curved cornea would be indicated. Secondly it would be possible to mount a galvanometer mirror on such a contact lens just to one side of the cornea. There would be no possibility of such a mirror rocking during eye rotations, as might be the case if the mirror were attached directly to the sclera. Thirdly it would be possible to engrave suitable

marks either on the centre of the artificial cornea or to one side of it, or on the artificial sclera, at will, but as indicated above the method would only succeed if the contact lens precisely fitted the curvatures of the subject's eyeball, so that there would be complete absence of "backlash" between the eyeball and the contact lens.

Reference has already been made to the fact that whereas the corneal reflection moves less than the cornea itself, for a given rotation of the eye, the apparent rotation of the retina is double that of the cornea, because it is being viewed via the lens system of the eye. It may be useful to summarise the efficiencies of the other structures mentioned above.

TABLE

| *Structure* | *Efficiency* |
|---|---|
| Corneal reflection ... ... ... ... | 0·5 – 0·4 |
| Iris ... ... ... ... ... ... | 1·0 |
| Sclera ... ... ... ... ... ... | 1·0 |
| Retina ... ... ... ... ... ... | 1·9 – 2 |
| Scleral mirror .. ... ... ... ... | 3 – 4 |

It will be seen that according to the above table the scleral mirror provides the most efficient optical arrangement.

## SECTION 4: SOME SUITABLE OPTICAL ARRANGEMENTS

There are broadly two optical methods which may be adopted for determining the eye movements. One consists of photographing the movements after suitable magnification, by means of a cinema or other camera. The other consists in utilising two or more photoelectric cells and amplifying and recording the currents which are generated in these. The relevant pros and cons of these methods are difficult to assess but both should give satisfactory results. The first method has been used recently by Hartridge and Thomson, the latter method is in use by Lord and Wright. When their method is used the subject lies on his back, his head resting in a ring; suitable supports are placed on either side of the head; a mouth plate is also employed. In these various ways head movements are restricted. Actual head movements are recorded by means of an artificial cornea which is attached to a suitable fitting which clamps on one of the front teeth. Both head and eye movements together are recorded by causing rays of light from an ultra-violet lamp after reflection in the corneal surface to fall on two photo cells, in front of which are placed knife edges in order to cut off part of the reflected beam. When

the cornea moves the beams of light are deflected. In consequence more or less light falls on the photo cells. The voltages on the cells after suitable amplification cause excursions of the fluorescent point of light in cathode ray tubes, and these are recorded photographically in the ordinary way. Continuous records are obtainable. So far they have not devised apparatus which will record both head and head and eye movements at the same time, so that they have not obtained eye movements independently of head ones.

The present method used by Hartridge and Thomson consists of a low-powered microscope, which is attached to a plaster of Paris hat which fits on the subject's head. This hat also carries

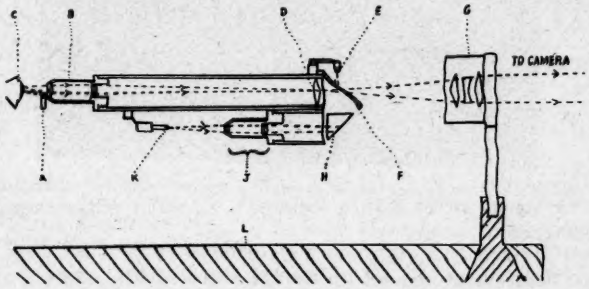


FIG. 1.

A plan of the original apparatus used by Hartridge and Thomson to measure movements of the eye.

A, light source to provide the corneal reflection; B, microscope objective; C, cornea; D, field lens; E, reference source; F, sloping glass plate to introduce reference image; G, collimator; H, right-angled prism; J, objective for the introduction of the fixation spots; K, source of light for fixation; L, optical bench.

the light source for illuminating the cornea, a reference source which is photographed alongside the magnifying reflection of the corneal image and a fixation light source, which by suitable optical means provides the subject with two bright points of light, on either of which at will he may preserve fixation. The low-powered microscope has such a focal length that the source of light, after reflection in the cornea and re-magnification, has approximately the same dimensions as the reference source. The latter is introduced into the light beam by two reflections at an unsilvered glass plate. In consequence two images of the reference source are seen by the camera. This duplication is found to assist the subsequent alignment and measurement of the photographic film. The cine camera which takes up to sixty frames per second is focused at

infinity, and the rays from the low-powered microscope attached to the subject's head, after passing through a field lens, enter a collimator lens which is attached to an optical bench. The optical bench to which the camera is attached is fixed to an independent

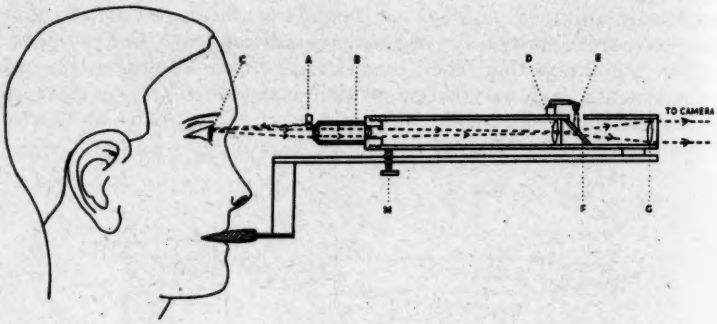


FIG. 2.

A plan of the new apparatus for measuring eye movements. Lettering as for Fig. 1, except that M indicates a screw for vertical height adjustment.

table, so that vibrations set up by the motor of the camera are not conveyed to the apparatus attached to the hat of the observer.

A new type of apparatus has recently been devised by Hartridge and Thomson, namely to hang from a suitable counterpoise a frame which carries the microscope, the reference lights and the

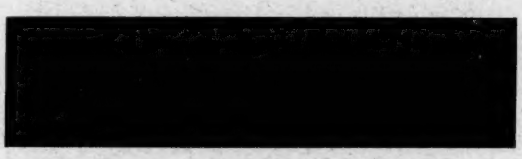

FIG. 3.

Five frames from a cine film taken at a speed of 64 frames a second, showing an intentional eye movement. The central frame shows the two reference images lying beside the moving corneal reflection.

corneal light source. It also carries a mouth plate which fits on to the teeth of the subject. The counterpoise is so arranged that the apparatus tends neither to rise nor to fall, but can be freely rotated in all directions. The optical apparatus is so disposed that the subject can observe uninterruptedly suitable fixation points of light which are attached to a wall beyond the apparatus. This

apparatus retains the advantage of the previous one, of enabling measurements of eye movements to be obtained which are quite independent of head movements. It has three other advantages. In the first place no constraint need be placed on head movements

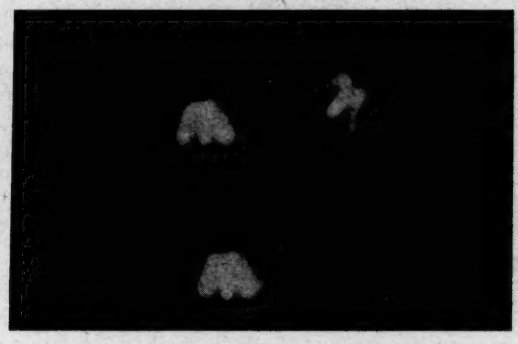

FIG. 4.

An enlarged image of a single cine frame from a strip of film taken during fixation of the eye. The corneal is the unpaired image on the right.

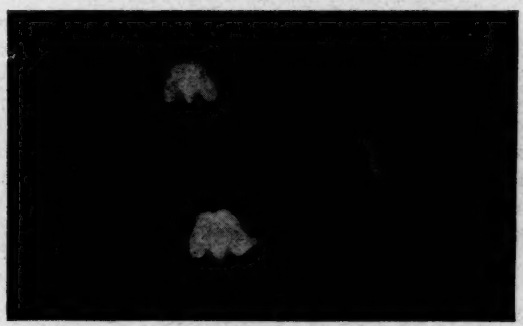

FIG. 5.

An enlarged image of a single cine frame from a strip of film taken during an intentional movement of the eye.

and no difficulties arise through attempting to immobilise the subject's head. In the second place the head movements relative to the camera may be determined by the movements performed by the images of the reference lights. Lastly since the optical equipment is not fastened to a plaster hat which rests on the subject's

head, fluctuations in vascularity do not affect the position of the apparatus in relationship to the eye.

A diagram of the old apparatus employed by Hartridge and Thomson and a diagram of the new apparatus now under construction are shown in Figs. 1 and 2. In Fig. 3 is shown an enlargement of a short length of cine film showing an intentional vertical eye movement. In Fig. 4 is shown an enlarged image of a single corneal reflection. Such fine definition would be impossible if the eye were performing very rapid vibratory rotations. Fig. 5 shows an enlarged image of a corneal reflection photographed whilst the eye was performing an intentional eye movement.

One millimetre on Figs. 4 and 5 corresponds to a displacement of the image on the retina equal to 28 $\mu$, that is, to 8·3 cone units.

## SECTION 5: THE EXAMINATION OF THE PHOTOGRAPHS

Three methods have so far been used for examining the cine film: (*a*) The detailed examination of single frames with a low-power microscope; (*b*) the projection of lengths of film on to a screen at one-quarter the speed at which they were taken; (*c*) the measurement of selected frames, using a microscope which has been fitted with a Leitz mechanical eyepiece micrometer. The latter method was found to be very laborious.

A fourth method, which is to be tested as soon as the necessary apparatus is available, consists in the preparation of an enlarged negative of one frame of the film and then the projection of the magnified images of other frames on to this enlargement, the magnification used being the same as that employed during the making of the enlargement. This method requires a special microscope having two mechanical stages, one about 200-250 cm. above the other, between the two being mounted a projection lens of short focal length. On the lower stage is placed the film strip and on the upper one the enlarged negative. The projection lens, which magnifies about 8 times, now produces an image of the film in the plane of the enlarged negative.

Using the horizontal and vertical adjustments the corresponding parts of the images of the filaments of the reference lights are now superposed, and adjustments are made until an exact fit is obtained. Now if the frame and the enlargement are alike, the consequence will be that when the images of the reference light are in exact superposition the images of the corneal reflection will be in exact superposition also. If on the contrary they are unlike, owing to a rotation of the eye, then a movement either of the film strip or of the enlargement will be required in order to superpose first the images of the reference light and then that of the corneal light, and this movement will be a measure of the eye movement which

has taken place between the exposure of the frame from which the enlargement has been made and that now being examined. It is hoped that this method will enable the films to be examined with the required accuracy at a rate of about one frame every two or three minutes.

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## TISSUE CULTURES OF MOUSE LENS EPITHELIUM

BY

IDA MANN

*From the Laboratories of the Imperial Cancer Research Fund, London*

IT has been pointed out by Kirby[1] that if an attempt is made to grow the lens in tissue culture the only cells which survive and multiply are those of the subcapsular epithelium. This is to be expected since the lens fibres are fully differentiated and cannot divide. Kirby's preparations were made with the lenses of chicks. In the present experiments an attempt was made to grow mammalian lens epithelium in tissue culture.

### EXPERIMENTS

Mice were used, mostly of the inbred strain known as C3H. Lenses of young mice up to 10 days old were used first but proved difficult to plant out without infection. Lenses from embryo mice of the same strain were then tried,with greater success. The embryos used were in the later stages of the pregnancy and good results were obtained with full term embryos taken just before birth. With care uninfected cultures could be obtained in about 60 per cent. of the trials. About 70 cultures were made in all.

The culture medium which gave the best results had the following formula :—

| | | |
|---|---|---|
| Rat serum | ... ... | 1½ parts |
| Tyrode solution | ... ... | 1 part |
| Mouse embryo extract | ... | 1 part |
| Dist. water—1-2 drops per c.c. | | |

RESULTS

1. If the lenses were cultured free from all surrounding tissue and with intact capsules they survived for about 10 days unchanged, and no outgrowths occurred.

2. If the capsule was ruptured at the moment of planting it shrank and lens fibres and subcapsular epithelial cells were extruded. The lens fibres dissolved in the medium within the first 2-3 days. The capsule remained unchanged but the epithelium proliferated and grew away from it all round in a flat sheet of large globular clear cells. Fragments of the sheet tended to break away and float off, so that permanent preparations were hard to make. Most of the cultures were therefore photographed *in vivo*.

Differentiation could be seen in the cells of the culture around the tenth day, beyond which very few survived. The first stage of differentiation was shown by increase in the cytoplasm and movement of the nucleus to one side. In a few cells a further stage was reached, the voluminous clear cytoplasm apparently flattened so that the cell became bluntly pointed at both ends, the nucleus remaining applied to one side of the central part of the elongated portion of the cell. This movement of the nucleus to one side of the cell is the first stage in the process of normal differentiation of a lens epithelial cell into a lens fibre in the intact lens. It can be seen towards the equatorial region in horizontal sections of mouse and other mammalian lenses. The nucleus moves to the side of the cell next to the capsule, and the cell then elongates forming a lens fibre with the nucleus eventually equidistant from the two ends.

The accompanying figures are representative of the results obtained. Fig. 1 shows a stained preparation of a surviving intact mouse embryo lens at 6 days. The subcapsular epithelial cells stain deeply.

Fig. 2 shows a similar lens after 10 days survival. The staining is no longer uniform as most of the cells have disappeared over the anterior pole and the nuclei are pyknotic elsewhere.

Fig. 3 shows a mouse embryo lens growing in tissue culture at 3 days. The capsule was ruptured at the time of planting. Débris of lens fibres and beginning sheets of subcapsular epithelial cells surround the shrunken and wrinkled capsule.

Fig. 4 shows a culture at 6 days. The sheet of outgrowing epithelium is wider.

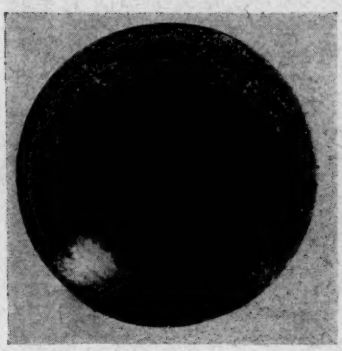

FIG. 1.

Intact surviving mouse embryo lens at six days, fixed and stained.

FIG. 2.

Intact mouse embryo lens in culture at 10 days. Fixed and stained. Many of the nuclei do not stain, many are pyknotic.

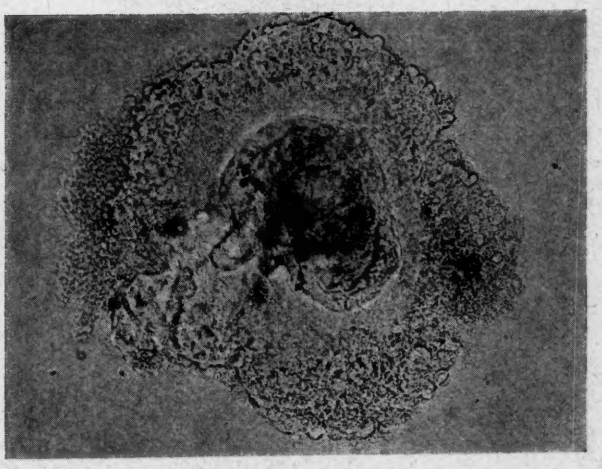

FIG. 3.

Mouse embryo lens with ruptured capsule in tissue culture at 3 days. Living preparation.

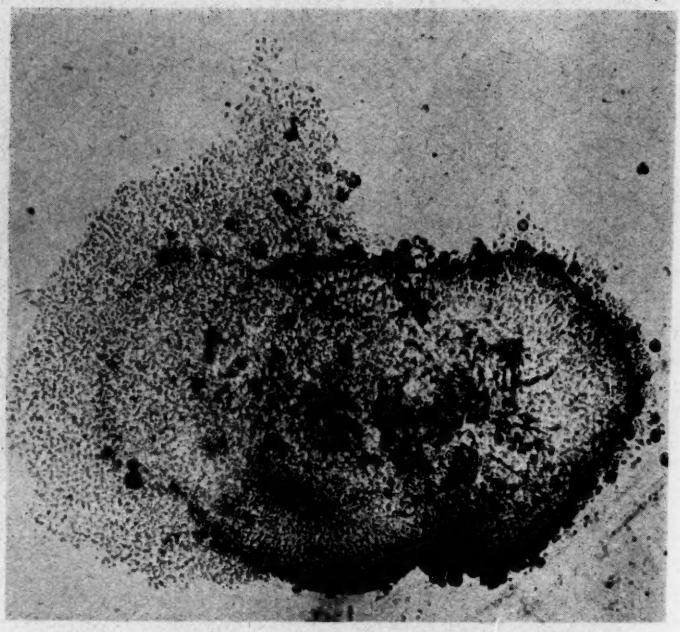

FIG. 4.
Mouse embryo lens with ruptured capsule in tissue culture at 6 days. Living preparation.

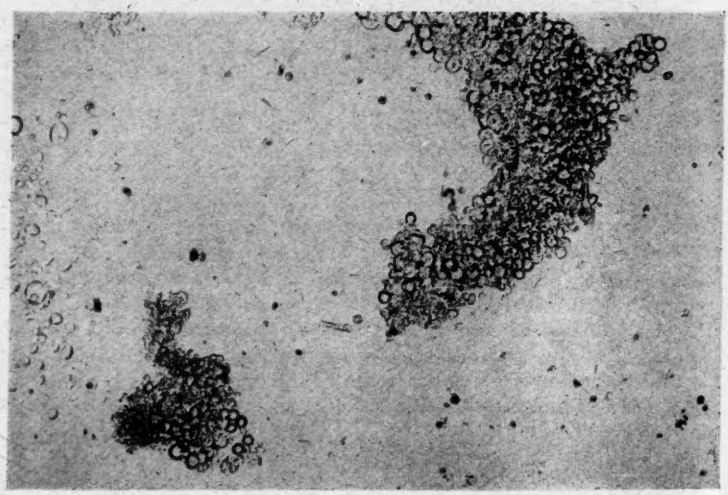

FIG. 5.
Portion of detached epithelial sheet from lens seen in Fig. 4. Living preparation.

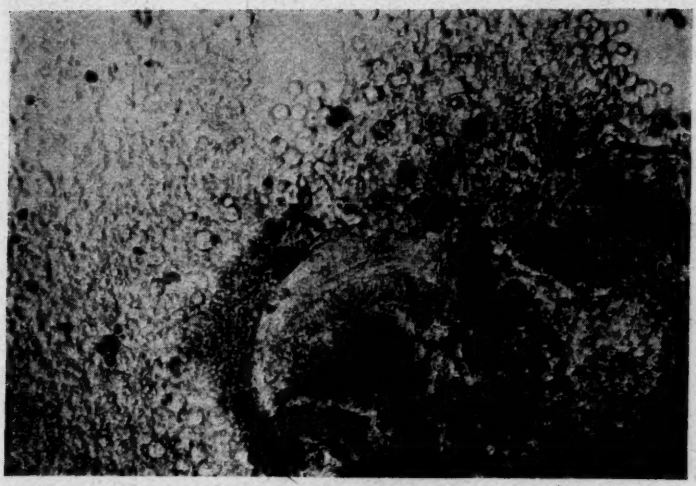

FIG. 6.

Full term mouse embryo lens growing at 11 days. Living preparation.

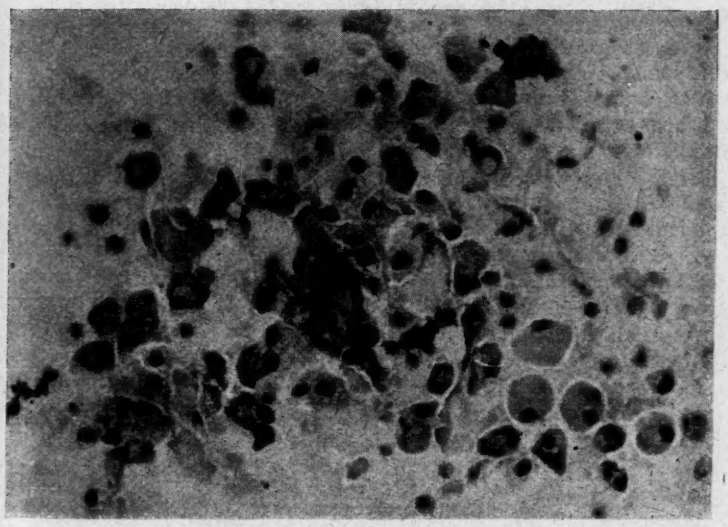

FIG. 7.

Epithelial sheet from mouse embryo lens tissue culture at 10 days. Fixed and stained with haematoxylin and eosin.

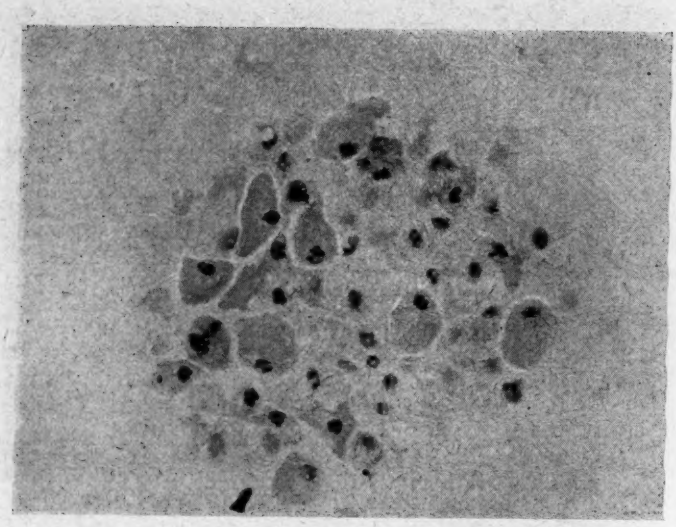

FIG. 8.

*Similar to Fig. 7, but showing slightly more cellular differentiation.*

*Fig. 5 shows a portion of the epithelial sheet which has broken off from the explant and is floating free in the medium.*

*Fig. 6 shows a higher power view of the epithelial cells growing out from the capsule at 11 days. The embryo in this case was full term.*

Fig. 7 shows an outlying portion of the epithelial sheet fixed and stained at 10 days. The position of the nuclei at the side of the cell and the large amount of clear cytoplasm is well seen.

*Fig. 8 shows another portion of a similar sheet in which two at least of the cells show an attempt at elongation at both ends away from the nucleus. No culture remained alive after 12 days and no further stage of differentiation was observed.*

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# COLOUR VISION, 1868 and 1948

BY

W. D. WRIGHT

IMPERIAL COLLEGE OF SCIENCE

"THE vast literature on colour vision consists almost entirely of papers written in support of some particular theory. It is peculiarly difficult to obtain a general and unbiased view of the subject, which demands a not inconsiderable knowledge of such diverse subjects as physics, physiology and psychology. I have here endeavoured to separate the best established facts of colour vision from the theories, and have then discussed the chief theories in the light of these facts."

In these words Sir John Parsons opened the Preface to his book "An Introduction to the Study of Colour Vision," and no more fitting comment could be made on the troubles that beset a student of colour vision. In a tribute such as this, it would be out of place to flog the merits of this or that theory, but it is intriguing to look back and compare the facts and theories of 1868 with those of the present day.

The year 1868 does not itself appear to be notable for any major scientific contribution to colour vision, but the period seems largely to have been dominated by the outlook of Helmholtz and Clerk Maxwell. That, of course, is equivalent to saying that the Young-Helmholtz theory was widely accepted, as a result of the colour mixing experiments described a few years earlier by both Helmholtz and Maxwell, and supported by the principles governing colour equations, as enunciated by Grassmann. Indeed, the Maxwell colour triangle had been described and the geometry of the triangle on the "centre of gravity" principle had been developed, while Maxwell had also given a very apt account of a three-dimensional method of specifying a colour in terms which would be very acceptable to many workers to-day.

The undue prominence apparently given to colour mixture data at that time was no doubt due to the fact that it was the chief sensory phenomenon on which fairly reliable measurements could be recorded. Three important methods of colour matching were available, namely the Helmholtz polarisation spectrometer in which the intensities of the matching stimuli were controlled by polarisation prisms, Maxwell's colour box in which slits of variable width in a spectrum provided the controls, and the colour top, in which the areas of each colour exposed on the top could be varied.

The physical energies of the red, green and blue lights used as

the matching stimuli were not known, but this was of no consequence in the development of the Maxwell triangle, since the units of the three lights were arbitrarily chosen to equalise the quantities of the three required in a match of a white light. It is rather interesting to realise that this basis for the units was almost forced on Maxwell by the lack of any other physical means of recording the intensities of the lights, and yet so effective has the system proved that it is firmly established at the present day and is embodied in the international C.I.E. system of colour specification.

This same difficulty of how to measure physical energies no doubt accounted for the absence of any measurements of the luminosity curve of the spectrum. Fraunhofer, it is true, had in 1817 published measurements on the brightness of different parts of the spectrum, but these results do not appear to have been followed up for many decades, while even at the end of the century, data were still being reported relative to the energy distribution associated with some particular light source rather than for a spectrum of known energy composition. Hence in 1868 the problem of actually sub-dividing the luminosity curve into three component parts had evidently not arisen.

Nevertheless, this was perhaps the hey-day of the trichromatic theory, when there was every promise that the main phenomena of colour vision would fit neatly into a simple framework of three independent receptor processes in the retina and three response paths from retina to brain, while the sketchy physiology of the time was simply inadequate to put the theory to a critical test. The theory, too, was well adapted to the mechanistic certainty characteristic of the Victorian era, before the subtleties of quanta, probabilities and statistics had invaded the scene.

Even so, the trichomatists were not unchallenged and in 1865, for example, Aubert's book, " Physiologie der Netzhaut," helped to restore the balance by the emphasis placed on adaptation and contrast phenomena, and by his insistence on four fundamental colour qualities—red, yellow, green and blue. This theme, of course, was later to be taken up by Hering, and Aubert's work may be regarded as the forerunner of the Hering school of thought. The failure on the part of the trichromatists to dissociate in their arguments the number of receptor processes from the number of distinct sensation qualities has been one of the most persistent causes of misunderstanding between the protagonists of the different theories.

What of visual physiology in 1868? Although the reddish coloration of the retina due to visual purple had been noted in the 1850s, the actual discovery of visual purple by Boll dates from

1876, with Kuhne's more exhaustive studies following during the next few years. On the anatomical side, while Treviranus had described the rods and cones in the retina in 1835, and some 20 years later H. Müller proved that the rod-cone layer was the photo-receptive layer, it was not until the 1880s that Ramon y Cajal commenced the work that was to lay the foundations of our present detailed knowledge of the retinal structures. Still more elementary in 1868 was the knowledge of the electrical response of the retina, for the first electro-retinogram had only recently been recorded by Holmgren in 1865.

Perhaps the state of colour vision knowledge at that time can best be described as lop-sided and fragmentary, a condition naturally fertile to the conflict of ideas that was so soon to develop. The cut and thrust of argument and experiment which we associate with the end of the century acquired a tempo that must have been exhausting as well as invigorating and without our Parsons' " Colour Vision " we might well despair of ever seeing the period in perspective.

We know that an extraordinary interest in defective colour vision was soon to be shown and extensive experimental data were accumulated. With the rise of the Hering school, emphasis was switched to adaptation effects and the subjective appearance of colours, but in view of the lack of information even now about the photo-chemistry of the cones, attempts to explain these effects in terms of anabolic and katobolic processes were obviously premature.

By 1924, Parsons could write (" Colour Vision," 2nd edition, p. 205) : " If we rapidly survey the sections of Part I (dealing with The Chief Facts of Normal Colour Vision) we shall find that the quantitative relationships are best established for luminosity and colour with the photopic fovea and for luminosity with the achromatic eye. When we consider peripheral vision, temporal and areal effects, both for photopic and scotopic vision, the quantitative relations are far less well established. The same grouping applies to Part II (dealing with the Chief Facts of Colour Blindness)."

This, surely, could also be written in 1948. Tangible and important advances have, of course, been made in the purely physiological aspects of the histology, photo-chemistry and electro-physiology of the retina, but to what major advances can we point on the visual and subjective side? Our experimental techniques are certainly better—we have better light sources, we can measure the physical energy of our light stimulus, we have improved optical equipment such as spectrophotometers, colorimeters, colour filters, photometer wedges and filters—so that we can now control and specify the conditions of our experiments with

greater precision. This has led to more accurate colour and luminosity measurements resulting in the international adoption of standard luminosity and colour mixture data, which have in turn enabled the observing conditions of an experiment to be defined more definitely.

These can be claimed as advances, but they are technological rather than scientific, and as contributions to colour vision theory do not take us much farther than the Helmholtz-Maxwell era. Perhaps this is inevitable; perhaps we must resign ourselves to still further delay until we have more exact and direct information about the physiological processes in the retina.

In another sense, too, we have advanced. As the late Professor Selig Hecht said at the Colour Vision Conference at Cambridge in 1947, we are at last beginning to grow up. We are acquiring a confidence in our measurements that was lacking before. We no longer regard points which lie off a smooth curve as necessarily erroneous observations, but are prepared to draw curves with humps in them. We no longer regard the scatter in our observations as an annoying inaccuracy, but rather as a significant measure of discrimination ability which, when analysed statistically, may lead to useful information about the processes of discrimination.

We have a clearer idea, too, of the nature and intricacies of the subject. Mostly we remember to distinguish between the physical stimulus, the physiological reaction and the psychological sensation. Our concepts are sounder; we recognise the need to describe the conditions of stimulation and to control the observer's state of adaptation. All this is at last becoming instinctive and in this respect we credit ourselves with a superiority over our predecessors.

Yet how much of the credit should go to Sir John Parsons! In his writings and conversation he has continually reminded us that our outlook must be broad. To the physicist he has had some hard things to say. Thus in his Thomas Young Oration (*Trans. Optical Soc.*, Vol. XXXII, p. 165, 1930-31): " Physicists cannot afford to ignore the teaching of physiologists. Physicists have been and are often now supercilious of the relatively inexact sciences, such as physiology, medicine and psychology. Let them ponder upon this indisputable fact—that all their measurements are founded upon their powers of sensory discrimination. They have been let off very lightly for their comparative neglect of this fundamental fact. It is a sheer piece of luck that they quite empirically hit upon the finest of all forms of sensory discrimination, *viz.*, contour discrimination, and applied it in the form of the vernier to their instruments."

However, as the physicist is recovering from this admonishment,

he is delighted to read a few paragraphs later: " I have already criticised the failure of physicists to pay sufficient attention to physiology. *Per contra,* I much doubt if there are many physiologists who really understand the remarkable juggling feats of König, Helmholtz, Abney and other physicists."

These are pretty sharp stimuli, and if we would do honour to their author, we cannot do better than respond as he would wish. There is no very obvious sign in 1948 that all the remaining colour vision problems are about to be solved; our aim must be to fill the gaps with experiment rather than theory, and to make sure that our experiments are designed on sound principles such as Sir John Parsons would approve.

## THE FIRST IRISH OCULAR PATHOLOGIST

### Arthur Jacob—(1790-1874)

BY

L. B. SOMERVILLE-LARGE

DUBLIN

IT is fitting that Arthur Jacob, the first Irish ocular pathologist, be recalled in this number of the Journal.

Although I can find no evidence in Jacob's biographies, or in his own numerous papers, that he ever actually practised any branch of medicine other than ophthalmology, he, like most of the medical giants of his age, was far from being satisfied by a mere speciality. He founded two ophthalmic hospitals, and took a leading part with others in founding both a medical school and a general hospital. He was joint founder and sole editor for 21 years of a medical journal. For 41 years he was a Professor of Anatomy and Physiology. Scientifically, he will be remembered as the first to describe the nervous layer of the retina (membrana Jacobi) and the rodent ulcer of the lids (Jacob's ulcer), and in the field of medical politics as a tireless fighter for medical reform, a dauntless champion of doctors' rights and a fearless opponent to all forms of quackery.

The details of his life need not detain us. Born in 1790 near the town of Maryborough (now Portleix), in Queens County (now Leix), the son of Dr. John Jacob, surgeon to the Queens County Infirmary, and grandson of Dr. Michael Jacob (Ballinakill), he came of a stock that had been in the midlands of Ireland for some centuries. The family was English and Jacob appears to have been a direct descendant of the Jacobs who had lived in Kent in the

13th century. The Irish branch was granted land in County Wexford in 1669, and one of the family fought in the Battle of the Boyne (1690) for King William (" of glorious, pious, and immortal memory "). Arthur Jacob served his apprenticeship with his father in Maryborough and under Abraham Colles (of fracture fame), in Steevens's Hospital, Dublin, proceeding to Edinburgh to graduate M.D. in 1814. Following graduation he travelled 960 miles on foot throughout England, visiting medical institutions, and ended by crossing to France and walking to Paris. He was proud of this characteristic feat, and it is a pity he left no account of it. Napoleon's escape from Elba (1815) hastened him back to London, where he spent some months in the departments of Sir Astley Cooper, Sir Benjamin Brodie and Sir William Lawrence. By attending Lawrence's clinic at the " Dispensary for Curing Diseases of the Eye and Ear " in Charterhouse Square, later the Royal London Ophthalmic Hospital, he became the first of many Dublin oculists to enjoy the " Moorfields outlook " in ophthalmology. A personal friendship developed between Jacob and his three famous teachers, and continued until the time of their deaths, Lawrence being one of the few ophthalmologists whose work he consistently praised.

Arthur Jacob from Dublin was thus attending England's first eye hospital in the same year as were Edward Delafield and John Kearney Rodgers from New York. There is no evidence that they got to know each other, but it is at least an attractive guess and made especially so by their subsequent rôles as founders of eye hospitals.

On returning to Dublin Jacob became an anatomical demonstrator to James Macartney, F.R.S., " the greatest anatomist and physiologist that Ireland has produced," and at that time Professor of Anatomy in the University of Dublin. While there he added much to the anatomical museum which Macartney later sold to Cambridge University. It is worth noting that Jacob's work for the museum was that illustrative of the absorbent system, his interest in this if not started was no doubt stimulated by his period in London with Sir Astley Cooper, then deeply engrossed in the subject. After two years' work with Macartney, Jacob wrote his famous description of the nervous layer of the retina (1819). In 1817 he commenced clinical ophthalmic work in Sir Patrick Dun's Hospital. In 1826 he was appointed Professor of Anatomy and Physiology to the Royal College of Surgeons in Ireland, and was on three occasions elected its President. After forty-one years' whole-hearted devotion to the interests of the College he resigned, and while still actively fulfilling his professorial duties, retired to Barrow-in-Furness in Lancashire, where he died five years later

(1874) at the age of eighty-five. He became Member of the R.C.S.I. in 1816, and in 1863 had the M.D. (Hon. Caus.) granted him by Dublin University.

## MEDICAL FOUNDATIONS

The 19th century was in Dublin, as elsewhere, a period of hospital foundations. Seven institutions were started in the city between 1814 and 1872 for the cure of diseases of the eye. Arthur Jacob founded two of them and his son (A. H. Jacob) one. When only twenty-seven years of age, and after little more than twelve months' residence in the city, Jacob founded in Kildare Street Dublin's second ophthalmic hospital—" The Charitable Institute for the Cure of Diseases of the Skin and of the Eye " (1817). This foundation was but three years after Dublin's first ophthalmic hospital had been opened by Commander Ryall, and twelve after Mr. Saunders had founded England's first ophthalmic hospital, later to become the Royal London Ophthalmic Hospital. Jacob thus was early in the field with his first eye hospital, beating Delafield and Rodgers foundations of New York's first eye hospital (the New York Eye Infirmary) by three years. The " skin " side of the institution was not handled by Jacob but by his dermatologist chief Professor Macartney, and was discontinued after a few years when the name was changed to " The Institute for the Cure of Diseases of the Eye." In the same year, 1817, Jacob and Macartney were " given permission to see eye and skin cases respectively in one of the empty wards " of Sir Patrick Dun's hospital. This appears to be the first purely ophthalmic appointment to a general hospital in Dublin. Jacob carried out operations for cataract in his Institute, but does not appear to have done any teaching there. He closed this hospital after six years to found, with the great Dr. Graves and others, the Park Street Medical School. This became one of the most famous of Dublin's private Medical Schools. A contemporary account of the school from the Lancet of 1825 on the occasion of Jacob's giving the opening lecture recalls it vividly : " Tossed to and fro, like a ship in a gale, we ascended to the theatre, and soon found ourselves seated amidst a dense multitude, where we could easily perceive that neither elbow room nor liberty of conscience was to be expected . . . a neat theatre, originals and imitations both in abundance; here lay a fish that would have made a gourmand's teeth water; there a copperplate, almost making the shadow as real as the substance itself; while between them rose skeletons in the naked majesty of bare bones and pride of varnish."

Jacob left Park Street Medical School two years after its foundation on his appointment of Professor of Anatomy and Physiology

to the R.C.S.I. (1826). In the same year he was elected to the full staff of Sir Patrick Dun's Hospital, which post he retained for the next 27 years. As, however, this hospital was wholly medical and as Jacob's appointment was a " surgical " one, it is unlikely that he did more than act in a consultant capacity—and perhaps see out-patients there. Certainly three years after his appointment he founded his second eye hospital—" The Ophthalmic Hospital," 1829, in Pitt Street (now Balfe Street). Here Jacob gave " clinical instruction " and " taught operations " for the modest fee of three guineas for three months. This little hospital was maintained and run solely by Jacob and has the distinction of being the only hospital in Dublin that during its entire existence was exclusively devoted to diseases of the eye. After some years as Professor of Anatomy and Physiology, Jacob, feeling the College was handicapped by the fact that many of the Staff were unattached to any teaching hospital, joined with his colleagues as the prime mover in the foundation of the City of Dublin Hospital (1832). There he had beds and taught clinical ophthalmology for twenty-four years. This, the last of his foundations, was the only permanent one and remains to-day as " The Royal City of Dublin Hospital." On its opening Jacob closed his Ophthalmic Hospital in Pitt Street.

## MEDICAL EDITOR

Jacob's contribution to foundations for the practising and teaching of ophthalmology, extensive as they were, are overshadowed or indeed wholly forgotten by his work as a fighter for medico-political reform. He became in 1837 assistant editor to the Dublin Journal of Medical Science but had to relinquish this post probably due to his personal attacks on medical colleagues. Two years later he founded with Henry Maunsell the " Dublin Medical Press," and remained its editor and inspiration for 21 years. This Journal later moved to London, and it still flourishes under the changed name of " The Medical Press and Circular." Although we know that robust language was at that time common in medical controversy, the force of Jacob's editorials and medico-political articles make strange reading to us a century later. He assails a professorial rival with " the chronic medico-literary diarrhoea under which the learned Professor has so long laboured," " the heterogeneous discharges with which he inundates the journals," " the foetid ichor which distills from such a quill." The editor of the Lancet (1841) is no less outspoken. " Messrs. Jacob, Maunsell, Porter, all the rag, tag and bobtail of the College School, hatched in corruption, though they still linger about the dunghill that gave them birth." In the heat of medico-political conflict to-day it is

well to remember that our medical forebears thought equally strongly a century ago. It is also of interest when reviewing the momentous medical changes of to-day to recall that Jacob in " The Medical Press," although strongly advocating the central control of local charities was anxious to retain the element of " charity," and foresaw danger in establishing a " centralised iron-bound medical service." The Medical Press keenly supported the Medical Act of 1858, but resented the improved status it gave to apothecaries. All Jacob's fights for reform were for his profession and his College. He took up arms immediately if he considered that either were attacked or the smallest disrespect shown to them. Any suggestion of professional quackery or advertisement called forth his most vitriolic utterances, and amongst these he powerfully denounced the practice of " going snacks," the attractive term then used for what we now call " fee splitting." In 1839 he went so far as to print a list of doctors, many of them high in the profession, whose names appeared in commendation of proprietary articles. His literary output was immense. During the 22 years of this editorship none of the weekly editions of the Dublin Press failed to carry something from his pen. Jacob's medico-political speeches and papers, though perhaps failing from their very vehemence to carry conviction, can certainly never be said to make dull reading.

## MEMBRANA JACOBI

Jacob read his " Account of a Membrane in the Eye " before the Royal Society in 1819. At that time anatomists described the retina as consisting of two parts, " the medullary expansion of the nerve, and a membranous or vascular laver." the former being

" Membrana Jacobi "—the figure illustrating Jacob's original description in the eye of a sheep—*Philosophical Transactions*, 1819.

next the choroid and the latter next the vitreous. Jacob wrote: "It is not the nervous layer which I detach . . . because I leave the retina uninjured." Again he states that this membrane "besides being attached to the retina is also attached to the choroid coat." He therefore considered it to lie between the choroid and the retina. What, however, he described and illustrated and what is named after him, "membrana Jacobi," is not the retina but what we now know to be only its neural layer. If we were to replace the inaccurate clinical term "detachment of the retina" by "detachment of Jacob's membrane" we would be anatomically correct. To the end of his life Jacob himself never seems to have realised the true nature of his important discovery.

His method of demonstrating this membrane was to fix the posterior half of the eye to a piece of glass covered with an inverted glass sphere, the whole was filled with water so that the eye floated and the sphere acted as a magnifying glass. The preparation was then capable of being passed around the class for examination. That it was not wholly successful is suggested by the semi-serious account of one of Jacob's students in the Park Street Medical School (Lancet, 1825). "In some papers published in one of the periodicals, Jacob lays claim to the discovery of an undiscovered something in the eye; but not a creature we believe gives credit to the assumption. We were ourselves present when he attempted to describe this 'mare's nest,' but neither we, nor any of those around us, could see the imaginary creature." However, the anatomical world could see the "imaginary creature," and Jacob's discovery had world wide recognition.

His anatomical dissections of the eye were very delicate, and in a period with few optical aids it is intriguing to consider what part his undoubted myopia may have played both in these and in his interest in the study of the minute. In 1823 he read a paper entitled, "Inquiries respecting the Anatomy of the Eye," before the Medico-Chirurgical Society of London. Here he described and produced illustrations of the membrana pupillaris. In one case that he illustrated he had succeeded in injecting a single vessel of this membrane at the 9th month of gestation. His observations led him to refute the then prevailing theory (of Blumenbach) that this membrane disappeared by a rent taking place in its centre and the vessels contracting to the iris, his contention being the now accepted one that the membrane "loses its vascularity, becomes exceedingly thin and is finally absorbed." By removing the cornea he demonstrated what we now know as Descemet's membrane to have no resemblance to the cornea itself ("no two membranes can perhaps be more dissimilar") but to be of "precisely the same nature as the capsule of the lens."

He left his entire anatomical museum containing some beautiful paintings of the iris on ivory to the R.C.S.I.

## JACOB'S ULCER

" Observations respecting an ulcer of Peculiar Character which Attacks the Eyelid and Other Parts of the Face " appeared in the Dublin Hospital Reports for 1827. Here Jacob describes with

"Jacob's Ulcer" and Jacob's cataract needle, from the original illustration. (*Dublin Hospital Reports*, 1827).

comprehensive accuracy the condition now known as rodent ulcer (Jacob's ulcer). Time has added little to his original description, " the characteristic features of this disease are the slowness of its progress, the peculiar condition of the edges and surface of the ulcer, the comparatively inconsiderable suffering produced by it,

its incurable nature unless by extirpation, and its not contaminating the neighbouring lymphatic glands." He mentions local and general treatment only to condemn them, and his finding that early surgical removal offered the only hope of cure held for the best part of a century. Jacob was jealous of this paper and never failed to draw the attention of subsequent " discoverers " of this ulcer to it.

## As a Surgeon

As a surgeon Jacob is best remembered by his treatise on " The Removal of Cataract as Performed with a Fine Sewing Needle through the Cornea." Although this was published in 1850 he had previously written both of his cataract needle and the operation he recommended in 1827 (Dublin Hospital Reports). The needle is an ordinary round sewing needle (No. 7 in size), bent at the point. This bending Jacob did himself, and he states that five or six needles in a hundred would stand the bending without breaking. Makers' attempts to reproduce his needle he despises—however, it is illustrated in Weiss' catalogue of 1865—and he recounts in detail both how to bend it and how to fit it to a handle. Of the value of both needle and operation he is characteristically dogmatic. He writes that some despise the needle " because it has not the imposing appearance of a finely polished blade with ivory handle and silver ferrule," but warns those " fond of improving surgical instruments to suit their peculiar notions " that it must be exactly to his specification. He concludes, " of the superior qualities of this needle I have not the slightest reason to change my opinion. It is, I am satisfied, by many degrees the best for the purpose." Alas that time has proved him wrong. Of the operation for cataract extraction, then coming into vogue, he states that although " malicious persons will say that I advocate this operation (of needling) because I cannot perform that of extraction," it is " on account of its hazardous nature a disgrace to surgery." Few of us would disagree with him in those pre-anaesthetic days.

His dramatic description of an eye operation as carried out 120 years ago, recalling as it does so clearly the character of the surgeon, must be given in his own words. " I seat the patient in a chair and make him sit straight up or inclining, according to his height. If very tall I raise myself by standing on a large book or two, or on anything which answers the purpose to be found at hand. In my own place of business I find old medical folios answer the purpose well; operating chairs, although very imposing and calculated to produce effect, I have not adopted, not finding myself at ease with such things. When he is seated I lay the patient's

head against my chest, and placing the middle finger of my left hand on his lower and the forefinger on his upper eyelid, and gently holding the eye between them, I strike the point of the needle suddenly into the cornea, about a line from its margin, and there hold it until any struggles of the patient, which may be made, cease. There must be no hesitation here, for if the cornea be touched without fixing the point of the needle in it, the eye will turn rapidly and the surface will be scratched. I advise the operator to pause here for a moment, holding the eye firmly and steadily on the point of his needle, and if necessary to say a word of encouragement or remonstrance to the patient." How vividly one sees the patient " struggling " on the point of the needle while seeking composure through the surgeon's " words of remonstrance." Jacob broke the lens up strongly, and he states that absorption took place remarkably quickly, patients sometimes being able to read within ten weeks. It is interesting to note that he cites the frequent occurrence of post-operative vomiting lasting often for 24 hours, and attributes it to the action of the broken lens on the iris. Jacob did not coddle his patients, " the less of bed the better, and the sooner the drawing room is made the place of convalescence, the better also." Whatever time may have decreed in respect to his needle and operation, we can endorse his conclusion, " the truth, perhaps, has never been told with respect to the result of cataract operation and perhaps never may be told."

Jacob has left us accounts of two other operations—for trichiasis and entropion. That for trichiasis appears to be original, although perhaps the credit should go to the patient. He " drilled a needle into the root of the inverted eyelash and then held a lighted taper to it until the part into which it was inserted was burnt to whiteness." For entropion he advocated the horizontal splitting of the tarsus and then everting it with sutures as described by his contemporary, Sir Philip Crampton. Jacob vividly demonstrated one such case pre-operatively to his students, " observe her scalded turned-in lids, depressing countenance, with profuse tears warning me that I have to encounter a struggle in which physical force must be relied on more than persuasion." No wonder.

Jacob was a conservative surgeon. He disapproved of paracentesis (for inflammatory conditions), and strongly criticised iridectomy, an operation he never seems to have carried out. For the " muscle-cutting candidates for fame " he had nothing but scorn, assisted perhaps by the fact that Sir William Wilde wrote approvingly of it. In acute dacryocystitis he recommended opening the sac through the conjunctiva rather than through the skin.

## VARIOUS PAPERS

In 1843 Jacob criticised " an attempt to make the study of pathology into a distinct department . . . but why or wherefore no one can tell . . . it is the province of the anatomist, physiologist, the teachers of medicine and surgery and the clinical teacher." However, he not only was zealous in carrying out post-mortems, but in 1846 wrote a long paper entitled " On Diseases of the Eye as a Guide in the study of Pathology." In this he points out that due to the transparency of the cornea, the exposed condition of the conjunctival vessels and the easily seen delicate iris tissue, morbid processes are well observed and studied in the eye. In these, he writes, the " accurate observer has living proof of what he supposes may be going on in other places under similar circumstances, but which he cannot demonstrate until death enables him to expose the parts." A century later we find ourselves returning to Jacob's pathological concept of the living tissue undergoing morbid changes.

In the " Cyclopaedia of Practical Medicine " (1834), Jacob contributed long articles on " Ophthalmia " and "Amaurosis." When considering "Egyptian Ophthalmia " he mentioned that so heavily infected were the troops lately returned from the Middle East to Ireland that a special ward was opened for them in Steevens' Hospital under Mr. Colles. On " Amaurosis " he contributed over 18,000 words, and it must seem strange to us, living in an age that takes for granted visual examinations of body cavities, that neither here nor in his account of the membrane that bears his name, nor in his writing on retinitis, did he ever consider the possibility of actually seeing the fundus of the eye.

Helmholtz made his fundamental discovery in 1850 and Jacob's contemporary in Dublin, Dr. H. Wilson (the natural son of Sir W. Wilde), published his book, " Theory and Practice of Ophthalmoscope " in 1868, yet I can find no suggestion that Jacob himself ever saw the ocular fundus. His first comment on the ophthalmoscope was in 1855, " not one man in 20 will be able to manage this instrument," and a year later he writes, " all we ask about the ophthalmoscope is that performers on it will not require us to believe all they say as to what they see through it." Jacob's famous rival, Sir William Wilde, showed an equal lack of enthusiasm, and he also never appears to have seen the human fundus.

In 1848 Jacob published his only book, " A Treatise on the Inflammation of the Eyeball." In spite of Mackenzie's classical text-book this uninviting, poorly printed, unillustrated pocket-sized volume seems to have had a real popularity in Dublin. There is reasoning in it beyond its time. Jacob repeatedly insisted that in

" iritis " all the uveal tract must be considered to be involved. He denounces wholesale cupping and, in opposition to Mackenzie, denies that inflammation takes place in the lens. He draws attention to social conditions among the poor (" badly fed, improperly clothed and miserably lodged ") as a cause for ocular inflammation. And flies in the face of accepted custom by criticising the well to do who follow " the usual unhealthy practice of sleeping in a bed hung round with curtains to exclude light and confine foul air," in bedrooms, " more like the crowded storerooms of furniture dealers than apartments provided for human beings." Jacob would assuredly be in the forefront of social medicine to-day.

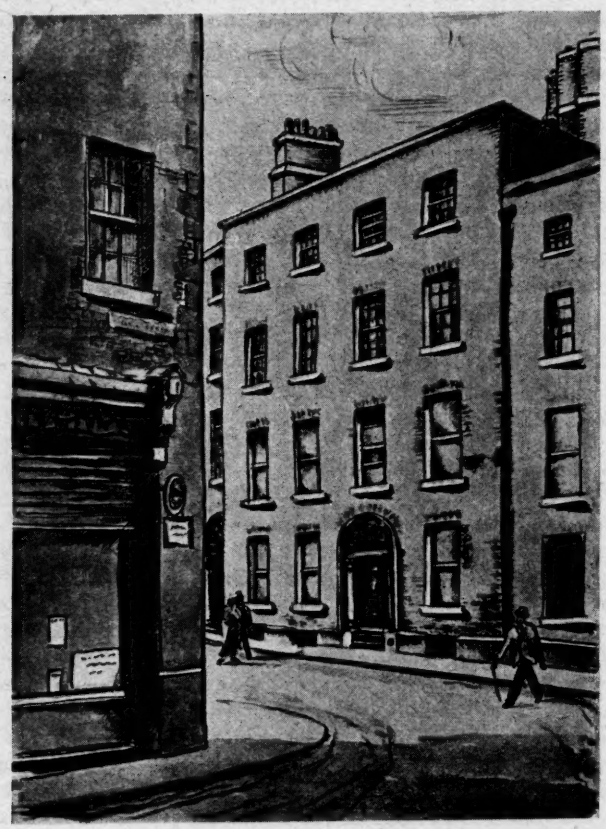
Jacob's mechanical bent is shown by a paper on a " Proposed Improvement in the Construction of the Cistern of the Portable Barometer " (1826). Instruments incorporating this suggestion were constructed. He also wrote and illustrated " A Description of an Apparatus for Injecting the Absorbent Vessels " (1825), a mechanical problem that intrigued him for many years. Comparative anatomy always interested him. One summer he heard that a dead whale, found floating off the West coast of Ireland, had been seized by the officers of the Admiralty. Although " probably six weeks dead and the weather being warm it provided a most uninviting subject for dissection "—he dissected it while floating and brought back specimens for his museum. Another time he made haste to buy a whale that had been washed ashore on Killiney Strand, near Dublin, and dissected it there. He wrote on the " Intra-orbital Cavities in Deers and Antelopes," on " The Mammary Gland in Cetacea " and on Sun Fish, as well as accounts of these whales.

Jacob was so keen a clinical observer that one is hardly surprised to find him passing beyond the merely physical. In a long paper with a resounding Victorian title, " An Essay on the Influence of the Imaginations and Passions in the Production and Cure of Diseases " (1823), he embarks on psychology and boldly advocates " that the power of the imagination and passions extensively influences the ordinary operations of the animal economy, and that the same influence is not only capable of producing diseases but of contributing to their removal." We are only now commencing to realise the truth of his assertion—" I fear, however, that our knowledge of the animal economy is far too limited to enable us to decide what diseases may or may not admit of cure from an impression of the mind." It is characteristic of Jacob's scientific approach that, unlike most of his medical contemporaries, he is not prepared just to sneer at the cures that he quotes in this paper as resulting from charms, amulets, and such like, but is prepared to give the whole subject serious consideration. This interesting

contribution is a clear call, made 120 years ago, for psychological investigation.

## THE MAN HIMSELF

Arthur Jacob lived in a large five-storied Georgian house in Ely Place (No. 23)—a quiet street of good houses and wealthy inhabitants. His house was half way between his two centres of interest—his hospital (The City of Dublin) and his College (The Royal College of Surgeons), a pleasant walk of half a mile from each. No doubt this assisted him in his almost invariable custom

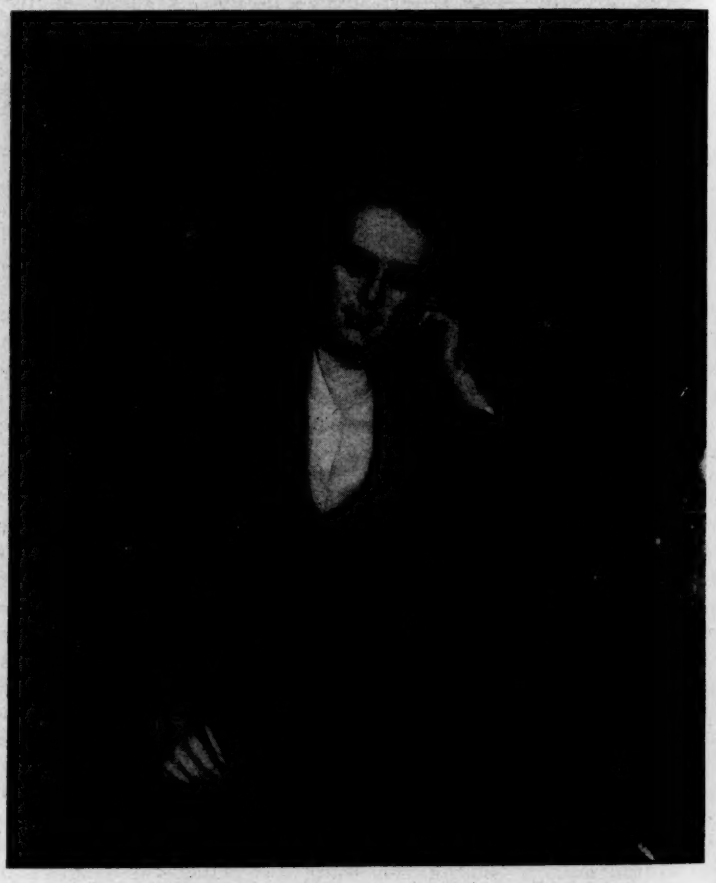


Arthur Jacob's house—23, Ely Place.

of commencing hospital work at 8 o'clock in the morning. All his life he was a man of great physical energy, nothing else could have permitted him to get through his hospital work, his "punctual and energetic professional duties," "his extensive private practice," and his large weekly literary output. His son tells us that his custom was to retire to bed after dinner (a 6 o'clock meal in the Victorian era), for a few hours' sound sleep, then to arise and "after tea" to spend most of the night reading and writing. Dr. Van Loon, physician and friend to the artist Rembrandt, is stated to have said that he could judge of a patient's character by the books at his bed side. Jacob's library of some 1,500 books he left to his college. It is not all composed of scientific volumes. There are also many books of travel (although once settled in Dublin Jacob never seems to have gone farther than London and that only very seldom), and many on the scientific aspects of agriculture (although as far as we know he never farmed), but perhaps stranger still are numbers of volumes of poetry, including the Odyssey and the Iliad. Something can surely be judged of a man by the library he makes, and on this assumption a surprisingly gentle side of Jacob is revealed.

The photograph reproduced is from a portrait done when Jacob was in the middle thirties. The membrana Jacobi was discovered, and Jacob's ulcer described. He sits at the corner of a table, sleeves rolled back, scalpel in hand, just about to divide an eye and mount it under the glass sphere that stands ready—thus to demonstrate his discovery. In the official portrait of him painted 35 years later for the Royal College of Surgeons he sits in much the same position in a similar chair at the corner of a similar table, his hair still curls and his very spectacle frames seem similar, but the face is lined and stern and the attitude uncompromising. At about the period of the younger portrait he is described by one of his students: "A gentleman of duodecimo stature so neatly habited that the affectation of the simplex munditiis could not disguise the assured indifference to toilet arrangements and exterior appearances. He was harnessed in a pair of spectacles so admirably fitted . . . that one might have mistaken the whole optical apparatus as the natural production of the parts . . . over the springs of this beautiful piece of mechanism hung two luxurious ringlets of beautiful auburn hair. . . . Around the medley of organs . . . there breathes a halo of kindness and conciliatory effulgence of good nature." We must agree that this account suits the portrait, but as the years passed much of the "halo of kindness" passed also, and he became as brusque and cantankerous in his manner as he became intolerably critical in his writing. Of a retiring disposition, a burner of the midnight oil and one who shunned even

the mildest convivialities, Jacob was undoubtedly an introvert. Although his aloof manner may have denied him many personal friends, his unselfish character earned him a score of sincere



Arthur Jacob—circa 1830.

admirers. He suffered from an ever present fear of showing the smallest suspicion of self-aggrandisement. This, as well as his intolerance of manner, is seen in his retort to the friends and colleagues who sought to honour him by a presentation. Knowing his feelings in this matter they were at some pains to decide on

something that he might accept. Finally, a medal was decided upon with Jacob's portrait on the obverse and suitably inscribed on the reverse. A gold one was struck for himself, a silver one for his brother (Dr. John Jacob of Maryborough), and bronze ones for the members of the presentation committee. These completed, the committee waited on the professor to request his acceptance (1860).

The Medal presented to Arthur Jacob.

Arthur Jacob's ink-bottle.

His reply is quoted by his son in " The Medical Press " (1874)— " I cannot accept of this or any other testimonial, but if at my death you still think that I deserve it, you may nail it on my coffin." History does not relate how he was persuaded, but persuaded he was, and a year later he attended a dinner held in his honour at the Royal College of Surgeons, when the medal was formally presented to him. His portrait was also ordered to be painted by the Council, and it hangs there to-day in the Examination Hall. His bust, too, is granted an honoured place in the college.

There is, however, another more personal reminder of Arthur Jacob's 44 years' work in the college. It is a mis-shapen penny ink bottle now mounted in silver and with an inscription which tells us it was his. If it shows the parsimonious character of the user it also shows the sincere respect of those that came after him. Men only do these things in memory of those they honour.

Jacob married Miss Sarah Coote Carrol in 1824, the same year as the Park Street Medical School was founded. He had five sons. The eldest (John Alexander) went into the church, the second (Samuel) became an oculist in Melbourne (Australia), the third (Arthur) was a civil engineer in Bombay and later in Barrow-in-Furness, the fourth (Archibald Hamilton) succeeded his father as oculist in Dublin and editor of " The Dublin Medical Press," and the fifth became an engineer in Travancore, S. India.

There can be no doubt that the ophthalmological tragedy of the 19th century in Dublin was the personal animosity of Arthur Jacob and William Wilde. Two dominant, energetic, and essentially intelligent men of wholly different character. The Wildes, Sir William, Lady Wilde (Speranza) and their son Oscar were spectacular extroverts. Wilson has shown us that Wilde himself was a *bon viveur*, kept a generous table, and rejoiced in the company of authors, scientists, nobility and peasants alike. He was 25 years younger than Jacob and died but two years after him, so that during almost his entire active life Jacob edited " The Medical Press." Yet the older ophthalmologist hardly ever mentions his brilliant young contemporary, and then only to condemn his work. Wilde writes a long, detailed, and most instructive report on the condition of the " Union Poor House Hospital " in Tipperary. This calls forth from Jacob an editorial headed sarcastically " Wilde's Pastoral," severely critical because Wilde outlines the treatment of ophthalmia to the local medical officer and thereby offends Jacob's idea of professional dignity. Again an American doctor visits European clinics and Jacob sneers, " in Dublin he is sure to dine with Dr. Stokes and sup with Surgeon Wilde." (We cannot refrain from envying this American wanderer). He never

mentions the internationally known eye hospital (St. Mark's Ophthalmic Hospital), founded and run by Wilde, nor does he give any notice to Wilde's innumerable scientific articles. Wilde, when editor of "The Quarterly Journal of Medical Science," deals more kindly with Jacob "if we were writing as historians simply and not in our editorial capacity, we might offer some remarks of the tone and style of 'The Dublin Medical Press'—but under existing circumstances we deem it more proper to refrain."

For forty years these two men dominated the ophthalmology of Dublin, and who can doubt that had they but combined in its organisation and scientific advancement the gain to the nation's medical life would have been great indeed.

*Without the enthusiastic assistance of Professor Widdess, M.A., Librarian and Lecturer in Biology at the Royal College of Surgeons in Ireland, and of Miss O'Brien, Assistant Librarian at the Royal College of Surgeons, the writing of this paper would not have been possible. To both I tender my sincere thanks. I am also indebted to Prof. Moorehead, who very kindly advised me over Jacob's association with Sir Patrick Dun's Hospital. Dr. Greene, of Norwich, a descendant of Arthur Jacob's was good enough to supply me with the photograph of Jacob's portrait that is in his possession. Mr. W. R. Jacob (London), Mr. R. F. West (London), Mr. Prior-Kennedy (Darlington), and Mrs. Kennedy (Tullamore) have all put me in their debt by personal communications on their ancestor. I am greatly obliged to Miss Thompson who went to much trouble to produce these excellent photographs.*

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# RADIOTHERAPY OF MALIGNANT INTRA-OCULAR NEOPLASMS

BY

H. B. STALLARD

LONDON

THE value of radiotherapy for glioma retinae is established. This tumour is very radiosensitive and when a quadrant or less of the retina has been affected by the growth treatment by radon seeds has caused the tumour to disappear and in a series of such cases treated at St. Bartholomew's Hospital there has been no recurrence in a period of follow-up from 1929-1948.

The results in the treatment of malignant melanomata by radon seeds are less fortunate. Metastatic carcinoma of the choroid is very radiosensitive and in some such cases it may be justifiable to use this treatment to conserve a little vision or to lessen the misery of the remaining months of the patient's life.

We have tried to strike the neoplasm with a dose judged to be adequate for its destruction without producing irremediable damage to the eye, and to bring the source of irradiation as close to the tumour as it is possible to obtain by surgical exposure. The insertion of a radon seed through the sclera into the growth has been abandoned for the technique of suturing radon seeds to the sclera over the site of the neoplasm, and we are now making trials with plaques of either platinum or silver 0·5 mm. thick containing radium salt and curved to fit the sclera neatly over the site of the neoplasm and fixed by sutures passing through holes in the edges of the plaque and thence through the superficial layers of the sclera. The advantage of these will be a more even and accurate distribution of irradiation than is the case with a straight radon seed fixed at a tangent to the surface of the sclera, and a source of supply which remains constant and is available for immediate use for owing to labour difficulties there is in England to-day a delay up to 10 days in obtaining radon seeds.

The transparency of the eye media affords us special opportunities in this work of assessing the exact size of the neoplasm, of marking its boundaries by surface diathermy coagulation at operation and of following up its subsequent behaviour.

## DOSE

For the permanent arrest and destruction of a malignant neoplasm it is necessary for the whole tumour-bearing area and indeed the tissues wide of this to receive a uniform intensity of irradiation effective for the particular growth during the whole time

of the treatment. In the absence of accurate knowledge as to the exact dose that the tissues receive it is safer to give the maximum dose that the tissues will stand without incurring the risk of serious destructive changes and complications. A sub-lethal dose may inhibit the neoplasm for a period of time but it inevitably recurs and the success of further radiotherapy is jeopardized. It is therefore necessary to arrange the radium or radon in such a way as to produce an adequate intensity and homogeneity of irradiation.

Gamma ray therapy is measured in terms of the ionization in the air by the radiation, and such measurements have been taken in post-mortem material using small Sievert condenser ionization chambers at various sites in a new growth which had been subjected to interstitial radiotherapy. The unit of intensity has been defined as " the intensity of the radiations at a distance of 1 cm. from 1 mg. point source of radium element (in equilibrium with its products) filtered by 0·5 mm. of platinum." One curie of radon is the quantity of radon in equilibrium with 1 gramme of radium and 1 millicurie is one-thousandth part of the this. The millicurie-hour intensity (I) is given by the formula $I \frac{m}{r^2}$ 1 mc. r is the distance in centimetres of the treatment point from the source and m is the strength of the radon source in millicuries.

" The roentgen is the quantity of x (or gamma) radiations which, when the secondary electrons are fully utilized and the effects of all scattered radiation avoided, produces in 1 c.c. of atmospheric air at 0°C and 76 cm. mercury pressure such a degree of conductivity that 1 electro-static unit of charge is measured under saturation conditions."

From practical experience to date it seems better to use radon seeds as close to the neoplasm as possible in the treatment of malignant intra-ocular tumours rather than the employment of massive doses delivered from radium needles set in plaques or the radium " bomb." Such large doses in most cases have had a destructive effect on the eye, at the worst causing its loss through corneal necrosis and panophthalmitis. Depilation of the lashes and eyebrows, a burn of the conjunctiva and irradiation cataract are lesser ills.

To-date the number of cases of malignant intra-ocular neoplasms in which radiotherapy was considered justifiable have been too few and the dose tried too empirical and experimental to give as yet definite advice on this point. As a temporary guide it seems that a dose of 3,500 r is adequate to destroy glioma retinae occupying one quadrant of the interior of the eye.

At present (1948) radon seeds 1 and 2 mc. are used and these are stitched to the sclera at appropriate sites in the case of intra-ocular neoplasms. Their active length may be varied up to 6 mm., their diameter is 1·4 mm. and the screen is 0·5 mm. of platinum.

The radioactivity of radon is reduced to half in 3·86 days, to one-fifth in 8·8 days, and at the end of 40 days only 0·07 per cent. remains. This decay factor is constant. One millicurie is destroyed in 133 hours. The seeds are left in place 4 to 8 days depending on the dose required.

I am grateful to Mr. F. S. Stewart, Radium Department, St. Bartholomew's Hospital, for the following description of his findings and for his help and ingenuity in designing a new radium applicator for the eye.

A review has been made of 22 cases successfully treated at St. Bartholomews' Hospital by radon seeds, in order to form an estimate of the radiation dose received at various points. In Table A the cases are arranged according to the size of the glioma. The dimension listed as "diameter" is measured along the spherical surface of the retina; the height is measured from the level of the retina and is an estimate since accurate measurement of this dimension is impossible.

TABLE A

*Radon Treatment of Glioma Retinae*

| Size of Growth | | No. and Strength of Radon Seeds (applied 168 hours) | No. of Cases Treated | Dose at Apex of Growth | Minimum Dose in Region of Tumour, at a level 1 mm. inside surface of Sclera |
|---|---|---|---|---|---|
| Diam. mm. | Height (Estimated) mm. | | | | |
| 3 | 2·5 | 1 × 2 mc. | 4 | 8800 r | 23400 r |
| | | 2 × 1·1 mc. | 2 | 9050 r | 22600 r |
| 4·5 | 3 | 1 × 2 mc. | 1 | 7050 r | 15700 r |
| | | 3 × 1·1 mc. | 1 | 10900 r | 30200 r |
| 5 | 3·5 | 1 × 2 mc. | 5 | 5800 r | 13900 r |
| 7 | 5 | 1 × 2 mc. | 4 | 3500 r | 9550 r |
| | | 2 × 2 mc. | 1 | 6300 r | 12900 r |
| 8 | 5·5 | 1 × 2 mc. | 1 | 3350 r | 7600 r |
| 10 | 7 | 2 × 2 mc. | 2 | 4350 r | 8500 r |
| 21 | 13 | 4 × 2 mc. | 1 | 2900 r | 12300 r |

In all cases treated with 2-mc. seeds:—

| | Where 1 Seed Used | Where more than 1 Seed Used |
|---|---|---|
| Maximum Dose at a level 1 mm. inside surface of Sclera | 38500 r | 50000 r |
| Maximum Dose where seeds touch Sclera ... ... | 125000 r | 150000 r |

The lowest dose received by any part of the tumour is at its apex and the value calculated is governed mainly by the figure estimated for the height. The apex doses shown are therefore only approximate, but they indicate that the smaller growths have generally received considerably higher doses than the larger. The fact that 7 successful results have been obtained with minimum tumour doses of 3,500 r or less suggests that the amount of radon could safely be reduced for diameters below 7 mm.

The dose received by the base of the glioma will, strictly speaking, depend on the combined thickness of sclera, choroid and retina at the site in question, but for simplicity the doses shown for the base are all calculated for a spherical surface 1 mm. inside the outer surface of the sclera. The dose at this level is very uneven due to the proximity of the seeds and reaches a maximum of 38,500 r in cases treated by a single 2-millicurie seed and approximately 50,000 r where several seeds were used. The minimum dose within the area of the dose is in most cases 9,000 r or more, as shown in Table A.

It is of interest to note that the outer surface of the sclera in direct contact receives as much as 125,000 r in single-seed treatments and 150,000 in multiple-seed treatments.

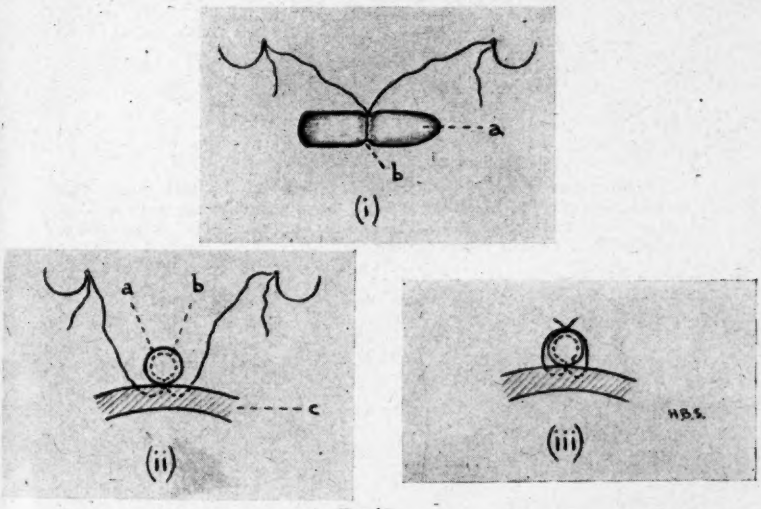



FIG. 1.

Diagrams drawn to show the method of suturing a radon seed to the sclera. (i) *a* Radon seed; *b* Fine black silk thread tied in a groove filed through the platinum envelope circumferentially about its centre. Arterial needles are attached to the free ends. (ii) The interrupted line represents the silk thread running in the groove around the radon seed and then passing through the superficial layers of the sclera, *c*. (iii) The ends are brought together over the seed and tied in the groove.

## TECHNIQUE

In 1929 Foster Moore inserted a radon seed into an intra-ocular neoplasm through a scleral incision made with an angular double-edged knife the exact width of which equalled the diameter of the radon seed. The point of the knife entered the base of the neoplasm and on its withdrawal a radon seed in a special holder was introduced point first into the incision. In the case of malignant melanoma of the choroid the solid growth was apt to be pushed on in front of the blunt tip of the radon seed. Fig. 1 shows the

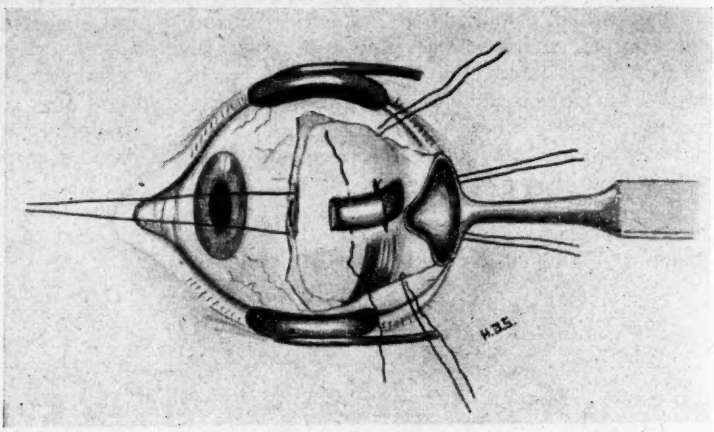


FIG. 2.

Glioma retinae of left eye at the temporal edge of the optic disc. The external rectus has been divided and the inferior oblique exposed. A stent strip moulded to the sclera and containing a 2 mc. radon seed is applied and held in place by two sutures.

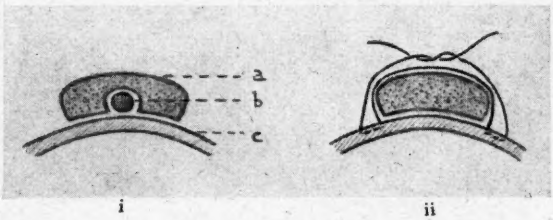
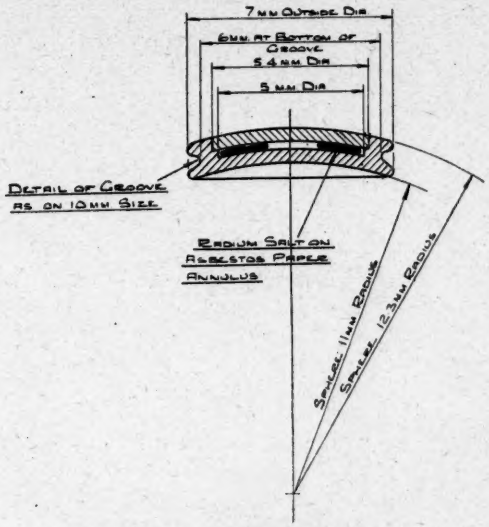



FIG. 2A.

i. Cross section through end of strip of stent holding radon seed; (*a*) Strip of stent dental wax moulded to sclera; (*b*) Radon seed embedded in stent; (*c*) Sclera. ii. Method of suturing stent strip to sclera in front of and behind equator.

technique I have used for suturing a radon seed to the sclera, and Fig. 2 that of suturing to the sclera a stent strip, with an embedded radon seed, or 2 seeds, so that the radon lies close to the optic nerve sheaths at a point where suturing the seed directly to the sclera affords considerable technical difficulties.

Fig. 3 shows a shallow platinum or silver radium container 0·5 mm. thick curved to fit the sclera and sewn to it.


7 MM OUTSIDE DIA
6MM. AT BOTTOM OF GROOVE
5·4 MM DIA
5 MM DIA
DETAIL OF GROOVE AS ON 10MM SIZE
RADIUM SALT ON ASBESTOS PAPER ANNULUS
SPHERE 11MM RADIUS
SPHERE 12·3MM RADIUS

Sectional view of eye applicator 5mm. in size.

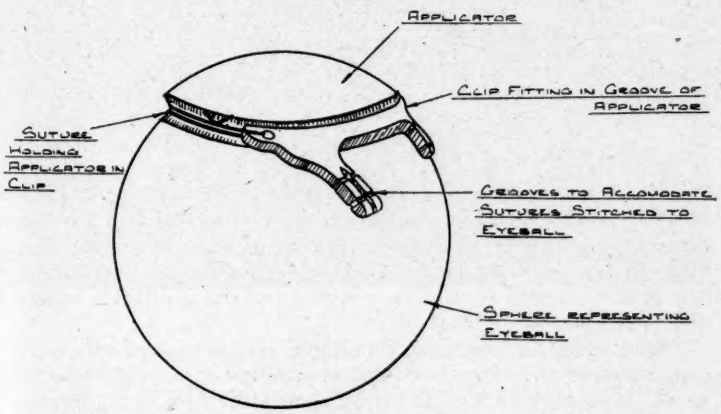

APPLICATOR
CLIP FITTING IN GROOVE OF APPLICATOR
SUTURES HOLDING APPLICATOR IN CLIP
GROOVES TO ACCOMODATE SUTURES STITCHED TO EYEBALL
SPHERE REPRESENTING EYEBALL

FIG. 3.

Radium applicator for attachment to sclera.

REACTION OF GLIOMA RETINAE TO RADON

About the third day after the application of radon, parts of the neoplasm, particularly at its periphery, become more densely white. The appearance is comparable to flakes of curdled milk,

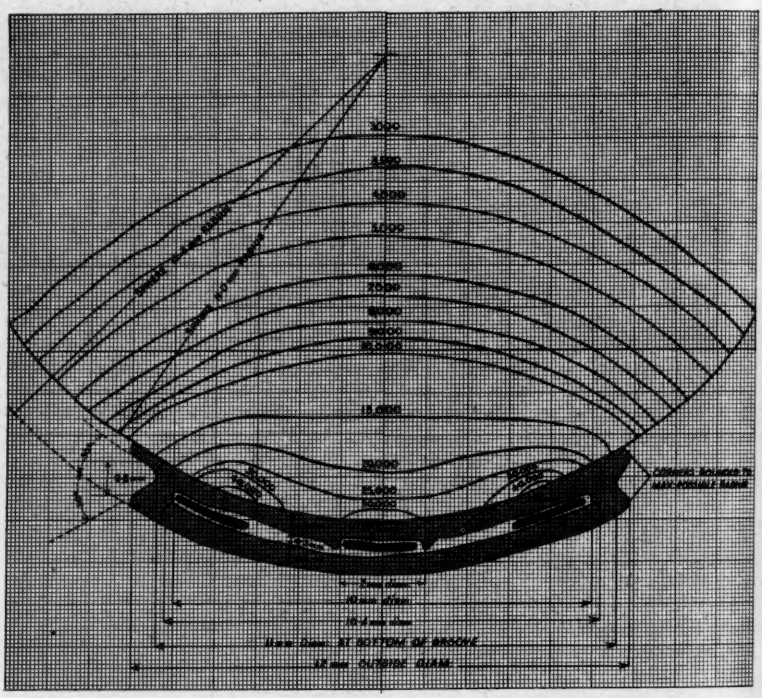


FIG. 4.

the glioma retinae looking like flocculent cream cheese in its preoperative state. In one or two weeks some of these dense white flakes become separated from the main mass of the neoplasm and the majority remain suspended near it. Rarely does such a flake gravitate in the vitreous to a place remote from the neoplasm, where it ultimately becomes absorbed.

Shrinkage of a successfully irradiated neoplasm is chiefly evident in the second and third week and continues till the eighth to tenth week. The periphery of the neoplasm is the first to be absorbed.

There may remain at the centre some greyish-coloured degenerative material for several months in cases where the neoplasm occupies about a quadrant of the globe. The scar at the site of application of a radon seed is characteristic (Fig. 5). It is flat, has a crenated edge fringed with pigment, and the centre is dense

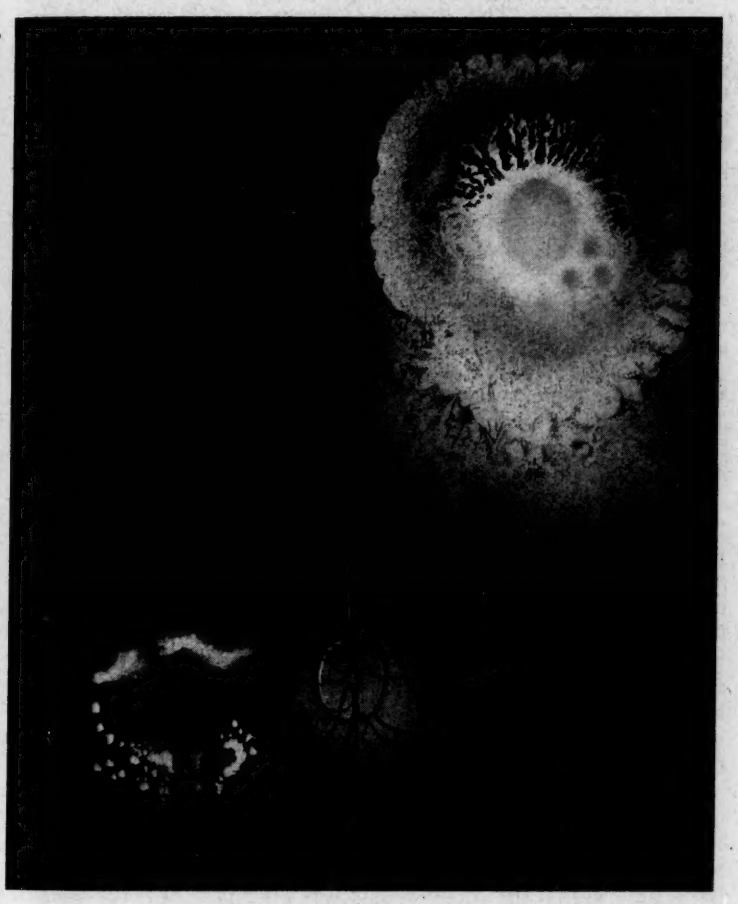


FIG. 5.

Glioma retinae. Right eye. Mass in upper nasal quadrant has been successfully irradiated. The scar in the retina and choroid is characteristic of an irradiated area. It has a crenated pigmented edge and the adjacent fundus shows fine pigment stippling. The retinal vessels are occluded in the upper nasal quadrant and some greyish exudates are around the macula.

white. The surrounding fundus is finely stippled as if peppered with pigment. The retinal vessels in the region of the neoplasm are occluded.

These changes are produced at the site of application of the seed. In a case of glioma at the left macula a 2 mc. radon seed was purposely placed away from the macula at the equator in the 2.30 o'clock meridian. The neoplasm disappeared from the macula leaving only a faint greyish discoloration, which was indeed difficult to detect in comparison with a normal fundus, whereas the site of application of the radon seed showed the characteristic changes described above and shown in Fig. 5. In the case of a large neoplasm a second application of radon may be necessary, but it is as well to wait for at least three months after the first application before deciding on this course.

For a description of the effects of radium on other ocular structures the reader is referred to Radiant Energy. (*Brit. Jl. Ophthal.*, Monograph Supplement, 1933.)

## RADIUM APPLICATORS

The use of radium in place of radon would be advantageous in avoiding the delay incurred in the preparation of the radon seeds. The conventional form of radium needle is, however, far too long for use in a similar manner to the seeds and it is proposed to use a new type of radium applicator as described below.

These applicators (see Fig. 3) have a platinum casing in the form of a segment of a spherical shell 1·3 mm. thick, the inner radius of curvature being 11 mm. to allow the device to be applied closely to the sclera. The casing is hollow, with a wall thickness of 0·5 mm., leaving a cavity 0·3 mm. in width. A range of sizes of applicator suitable for irradiating circular areas of the retina from 2 to 20 mm. in diameter is proposed, and according to the area to be irradiated, the cavity contains an asbestos paper disc or annulus (or both) impregnated with radium salt. The wall thickness of the casing is sufficient to absorb all alpha and beta radiation so that the irradiation is purely by gamma rays.

The applicator is secured by sutures to the sclera. A groove is made on the edge of the casing and a semi-circular clip, with projecting lugs which can be sutured to the sclera, is made to fit the groove. Several interchangeable clips of different lengths are made for each applicator so that the sutures can always be made near the equator, no matter in what part of the globe the glioma is situated.

The radium loading has been calculated to give a dose of approximately 3,500 r in one week (168 hours) at the apex of the growth. (For this purpose, the height of the glioma has been assumed to be seven-tenths of the diameter.) The distribution of the radium

over the surface treated has been chosen so as to make the dose as uniform as possible at the surface of the retina. Taking the 10 mm. diameter as an example, the dosage distribution is as shown in Fig. 4.

[The applicators are made by Messrs. Johnson, Matthey and Co., Ltd., to whom acknowledgment is made for collaboration in the technical aspects of the design.]

## CLINICAL FACTS

This series consists of 15 cases treated by the application of radon seeds sewn to the sclera over the site of the glioma. Twelve were treated at St. Bartholomew's Hospital and 3 at the Moorfields Eye Hospital from 1934-1948 (see Table A). There were 8 males and 7 females. Their ages were between 4 months and 3 years, 6 were under one year old, 6 between 1 and 2 years and 3 between 2 and 3 years of age.

Fourteen were bilateral and one unilateral. The right eye was treated by radon in 7 cases and the left eye in 8. The size of the neoplasm was over $\frac{1}{2}$ the interior of the globe in 1 case, nearly $\frac{1}{2}$ in 1, and $\frac{1}{4}$ in 2. There were 4 separate islands of glioma in 2 cases, 3 in 3 cases and 2 islands in 1 case. There were single masses of growth in 8 cases. The macula was the site of an island of growth in 4 cases.

It is important to search the periphery of the fundus very carefully, for small hemi-spherical masses about 1·5-3 mm. in diameter were seen at the ora serrata in 4 cases. Furthermore it is important to examine the fundus at monthly intervals for a few years to discover islands of glioma arising in parts remote from the original neoplasm treated by radon. Such were found in 3 cases, one 5 months after irradiation, another 4 months later and the third one month after the application of radon seeds to 2 islands of glioma.

The dose of radon and the number of seeds were planned according to the size of the neoplasm. In 2 cases a single application of one 2 millicurie seed was made; in 4 cases 3 seeds were used and in 1 case 4 seeds. Two applications were necessary in 6 cases and 3 applications in 2 cases; and 3 of these were for a new island of glioma arising at a later date and remote from the site of the original growth. In 4 instances the second and third applications of radon were made at the site of the original growth because the destructive effect of the initial application of radon was considered doubtful. Although the changes in the neoplasm made by effective irradiation were evident on ophthalmoscopic examination between the 3rd and 8th day after irradiation and the neoplasm may disappear in 1 to 2 months it is, in some cases of large masses of growth, necessary to wait 5 or 6 months after radon treatment to

be sure that the effect is complete. The site where the seed is sewn to the sclera shows in the fundus a characteristic white and pigmented scar with a crenated edge which appears about the 7th month and is well formed 14 months after irradiation.

If the seed is placed a little remote from the island of glioma, for instance about 3 mm. above or to the temporal side of a neoplasm about 3 mm. in diameter at the macula (as in Case 6), the site of the irradiated growth will appear as a faint greyish discoloration and the position of the radon seed be shown by the characteristic scar described above.

## COMPLICATIONS

(1) *Cataract.*—In 5 cases irradiation opacities occurred in the lens, in 4 of these the changes were in the centre of the posterior cortex and up to about 1·5 mm. in diameter. In case (11) opacities began 13 months after irradiation and over a period of 6 years extended slightly from the equator of the lens at 2.30 o'clock in direct line with a 2 mc. radon seed which had been sewn to the sclera at the ora serrata.

In the 4 children with central posterior cortical opacities 4 x 2 mc. radon seeds had been placed just behind the equator in one case; 3 x 1·1 mc. seeds at the macula in one case; in another case on 2 occasions at 3 months interval a 1·1 mc. seed had been placed above the optic disc a second 1·1 mc. at the equator and one year and nine months later a 2 mc. seed was placed below the disc; and in the 4th one 2 mc. seed and then 2 x 2 mc. at 6 months interval were placed over the macula and adjacent to the temporal edge of the dural sheath of the optic nerve. In these cases the onset of lens changes after irradiation was 2 years and 2 months, 11 years and 6 months, 4 years and 9 months, and 5 years and 9 months respectively.

In case (1) the lens opacities have gradually spread in the posterior cortex from 1936-1948 and together with peri-macular exudates vision has become reduced to 6/60. Despite this handicap he has completed his education at Manchester Grammar School and passed School Certificate.

(2) *Retinal changes.* (*a*) *Exudates.*—Greyish irregular-shaped flecks of exudate occurred at and around the macula in 5 cases. In 4 of these relatively heavy doses of radon had been used behind the equator, 4 x 2 mc. seeds in 1 case; in a second case applications consisting of 2 x 1·1 mc. were given on 2 occasions and 1 x 2 mc. on one occasion; applications of 3 x 2 mc. and 2 x 2 mc. in a third case; and in the fourth case one application of 4 x 2 mc. and 7 months later 2 x 2 mc. were used. In the fifth case one 2 mc. was placed above and to the temporal side of a macular growth. In this

last case the distribution of the exudates ultimately resembled those seen in retinitis circinata. The onset of these changes after irradiation was 2 years and 2 months, 1 year and 10 months, 11 months, 7 months and 9 years respectively. The exudates persist for a number of years, up to 11 years has been observed to-date. The occurrence of this complication has been noted in the series only when radon was used behind the equator. It has, however, been seen in a patient suffering from a lesion of haemangiogliomatosis retinae at the ora serrata which Foster Moore treated with radon seeds.

In one of these cases associated with central lens changes vision fell to 6/60, in another from 6/18 to 6/24 and the remaining 2 lost their sight through a severe vitreous haemorrhage in one case and total retinal detachment in the other.

(*b*) *Haemorrhages.*– Retinal haemorrhages were a late complication in 6 cases. In one instance 2 very small haemorrhages occurred near the equator in the upper nasal quadrant 3 years after irradiation of a neoplasm at the macula and these have persisted at this site for over 8 years. In the other 5 cases the radon seeds had been placed near the main branches of the central retinal vessels within a few millimetres of the optic disc and haemorrhages occurred 6 months, 7 months (2 cases), 11 months, and 1 year after irradiation.

In one patient, Case (3), the haemorrhage was so severe that it extended into the vitreous, causing retinitis proliferans.

(*c*) *Retinal detachment* occurred in 4 cases. In 2 of these the growth filled about half the eye in case (4) and more than this in case (5). Nearly half the interior of the eye was occupied by 4 islands in case (12) two of which were large. The dark greyish colour of the detachment suggested that between the retina and choroid there existed a mass of cell débris. In none of these cases followed up since 1936 and 1937 has there been any evidence of recurrence of the glioma.

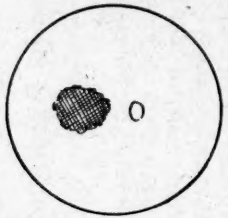
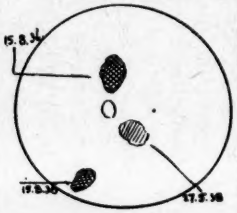
## RESULTS

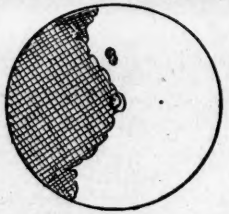
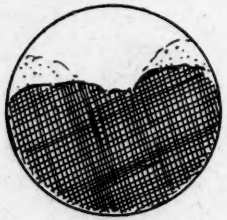
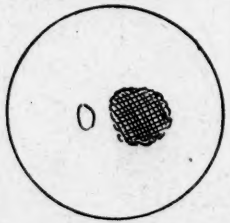
In all 15 cases the islands of glioma were effectively irradiated by radon seeds.

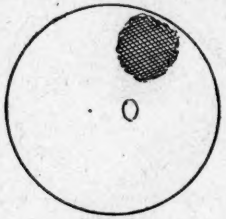
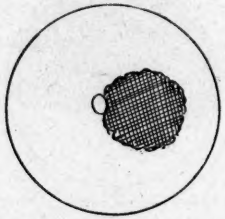
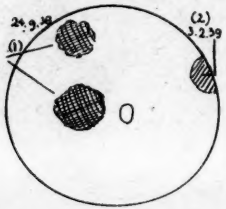
One child, Case (7), died about one year after successful irradiation of a single island of glioma, of which there was no trace on pathological examination after death. The cause of death was not discovered. It was suggested that it might have resulted from the cerebral effects of deep X-ray therapy given to the orbit from which the other eye had been excised.

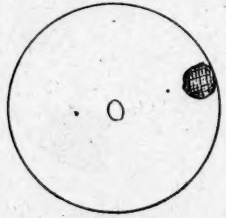
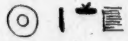
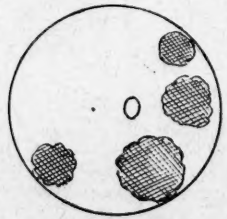
Case (10) was evacuated from St. Bartholomew's Hospital at the outbreak of war, went to Manchester and in January, 1940, on account of complicated glaucoma and the appearance of a suspicious mass near the optic disc the eye was excised.

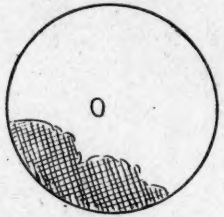
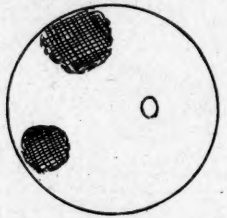
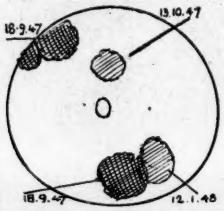
## TABLE B

| No. Initials and Sex | Age | Date of Radium Treatment | Eye Treated by Radon | Site and Size of Glioma Retinae | Dose in Millicuries | Complications | | | Results |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Cataract | Retinal Exudates | Other Complications | |
| (1) J.W. Male | 2 7/12 | 21.8.34 — 31.8.34 | R | | 4 × 2 mc. Post equator. 7 mm. apart. | 24.10.36 Central post-cortical. | 20.9.35 Peri-macular | — | 1944. R.V. 6/36. 1946. Passed School Certificate. 1948. R.V. 6/60. |
| (2) M.B. Male | 1 1/12 | 26.3.35 — 29.3.35 | R |  | 3 × 1·1 mc. Over macula. 2 mm. apart. | 2.9 46 Central post-cortical slight. | 15.4.38 — | 15.4.38. One small haem. upper nasal at equator. 2.9.46. Two haemorrhages at same site. | 1946. R.V. 4/60. At boarding school. |
| (3) M.M. Female | 4/12 | (1) 15.8.36 — 21.8.36 (2) 21.11.36 — 31.11.36 (3) 27.5.38 — 3.6.38 | L |   | (1) 2 × 1·1 mc. (2) 2 × 1·1 mc. (3) 2 mc. | 8.5.41 Post-cortical opacity slight. | 3.6.38 Macular | July 1937. Large haemorrhage above optic disc and macular. April 1939. Recurrence of haemorrhage, same site. | 1948. P.L. Schiötz. 32 Hg mm. Shrinking eye. |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (4)<br>P.R.<br>Male | 8/12 | (1) 11.1.37<br>— 21.1.37<br>(2) 23.7.37<br>— 30.7.37 | L |  | (1) 3 × 2 mc.<br>(2) 2 × 2 mc.<br> <br>Post equator.<br>7 mm. apart. | — | 10 12.37<br>Macular | 21.5.37. Retinal detachment. | 1948. Blind College, Worcester.<br>No recurrence.<br>Shrunken eye. Clear cornea and lens. |
| (5)<br>M.L.<br>Female | 1 5/12 | 25.10.37<br>— 2.11.37 | R |  | 3 × 2 mc.<br> | — | — | 25.5.38. Total retinal detachment.<br>Retinal haemorrhages ++. | Until 25.5.38 successful irradiation of glioma. |
| (6)<br>J.K.<br>Female | 1 6/12 | 27.2.37<br>— 1.3.37 | L |  | 2 mc.<br> | — | 15.3.46<br>Peri-macular like retinitis circinata. | — | 5.6.45. L.V. 6/18.<br>1.8.46. L.V. 6/24. |

| No. Initials and Sex | Age | Date of Radium Treatment | Eye Treated by Radon | Site and Size of Glioma Retinae | Dose in Millicuries | Complications | | | Results |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Cataract | Retinal Exudates | Other Complications | |
| (7) D.E. Male | 3 | (1) 12.4.38 — 19.4.38<br>(2) 22.10.38 — 29.10.31 | R |  | (1) 2 mc.<br>(2) 2 × 2 mc.<br> <br>Between equator and O.D. | — | — | — | Glioma, clinical cure.<br>1.3.39. Died. Cause unknown.<br>? Effect of deep X-ray. (for left orbit) |
| (8) T.M. Male | 1 5/12 | (1) 16.7.38 — 23.7.38<br>(2) 3.1.39 — 14.1.39 | L |  | (1) 2 mc.<br>(2) 2 × 2 mc.<br> <br>(1) Over macula.<br>(2) Seeds 7 mm. apart up to duxal sheath. | 26.4.44<br> <br>Post-cortical | — | 7.7.39. Retinal haemorrhage adjacent to O.D. | 27.4.45. L.V. 6/60.<br>1948. Reads and writes well.<br>Uses nasal part of retina for fixation. |
| (9) D.M. Female | 7/12 | (1) 24.9.38 — 11.10.38<br>(2) 3.2.39 — 11.2.39 | R |  | (1) 2 mc. between 2 islands.<br> <br>(2) 2 mc.<br> | — | — | — | Attends school.<br>Sees her way about. |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (10)<br>R.B.<br>Female | 1 | (1) 14.1.39<br>— 21.1.39<br>(2) 29.7.39<br>— 8.8.39 | L | | 1 mc. 2 × 2 mc.<br> <br>2 mc. 2 mm. above optic disc. | — | — | 18.7.39. Retinal haemorrhage 2 mm. long. Upper temporal edge of central neoplasm. | 3.1.40. Left eye excised in Manchester.<br>? Active growth at O.D.<br>Complicated glaucoma. |
| (11)<br>J.F.<br>Female | 5/12 | 7.2.39<br>— 11.2.39 | R |  | 2 mc.<br>  | 29.3.40<br> <br>4.2.46<br> <br>No further change | — | — | Illiterate.<br>Mentally backward.<br>"Sees well." |
| (12)<br>J.F.<br>Male | 2 | (1) 11.8.39<br>— 19.8.39<br>(2) 28.3.40<br>— 4.4.40 | R |  | (1) 4 × 2 mc. Seeds<br> <br>(2) 2 × 2 mc. on stent lower nasal quadrant | — | 25.3.40<br>Macular | 25.3.40. Haem. nasal side of O.D.<br>1948. Shrunken eye. Deep a.c. | 1948. Alive and well.<br>23.11.42. Blind School. |

| No. Initials and Sex | Age | Date of Radium Treatment | Eye Treated by Radon | Site and Size of Glioma Retinae | Dose in Millicuries | Complications | | | Results |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Cataract | Retinal Exudates | Other Complications | |
| (13) W.B. Male | 2 4/12 | 13.3.46 — 20.3.46 | L |  | 3 × 2 mc. 7 mm. apart. Post-equator. | — | — | — | 1948. Sees well. |
| (14) S.V. Male | 1 1/12 | 17.7.47 — 24.7.47 | L |  | 3 × 2 mc. | — | — | — | 12.4.48 Sees well. |
| (15) J.H. Female | 4/12 | (1) 18.9.47 — 25.9.47<br>(2) 23.10.47 — 6.11.47<br>(3) 22.1.48 — 29.1.48 | L |   | | — | — | — | 15.4.48. Sees well. |

Case (5) was the only unilateral case treated by radon seeds in this series. More than half the interior of the eye was occupied by the neoplasm. Excision of the eye had been refused by the parents. It seemed from ophthalmoscopic appearances that the neoplasm had been successfully irradiated. Seven months after this treatment a total retinal detachment and severe retinal haemorrhages occurred.

In Case (4) about half of the interior of the eye was filled with the neoplasm. Five months after irradiation the retina was detached at the site of the neoplasm and ultimately the eye shrank. The cornea and lens have remained clear to-date for 11 years, there has been no recurrence of the neoplasm and the boy has been in good health. He is doing well at the Normal College for the Blind, Worcester.

Case (12) had 4 islands of glioma, 2 of which were large. He had 4 x 2 mc. seeds applied in August, 1939, and one in March, 1940. In November, 1942, the eye became soft, shrunken, the anterior chamber deep, the lens opaque and there was no perception of light. To-date April, 1948, he is alive and well.

Four children (Cases 2, 6, 8 and 9) had neoplasms at the macula. In Case (6) a 2 mc. radon seed was purposely placed away from and above and to the temporal side of the neoplasm at such a distance that the growth was within effective range of the radon seed. As mentioned above the typical scar in the retina and choroid which occurs at the site of the seed did not in this case involve the macula. Except for slight greyish discolouration there was no ophthalmoscopic change at the macula until 9 years after irradiation when some exudate appeared. This child had 6/18 vision which has fallen to 6/24 on account of the exudates. It is interesting to note that vision has been sufficient for school work in the other 3 cases of macular involvement where a radon seed was placed over the macula and the characteristic scar appeared at this site. M.B. (Case 2) saw 4/60 and is doing well at a boarding school. T.M. (Case 8) sees 6/60 with the nasal part of the fundus, writes and draws clearly and reads fluently from a book held about 6 inches from his eye and to the temporal side. J.W. (Case 1), treated in 1934, had good vision until increasing posterior cortical opacities reduced this to 6/60. He has attended Manchester Grammar School and passed school certificate. The lens is to be extracted.

J.F. (Case 11) is illiterate and mentally backward, she attends school and it is evident that she sees reasonably well playing games. Of the remaining 4 children 3 are at present too young for accurate visual acuity tests, but it is clear that they see objects about them and when they have become old enough have been able to dress, feed themselves and join in games with other children.

To sum up. In this series there has been one death (cause unknown) whose eye was successfully irradiated. Four have become blind, in 3 of these the irradiated eyes shrank, one after a severe vitreous haemorrhage and retinitis proliferans and the other 2 after retinal detachment, and the fourth had her eye excised in Manchester because of a suspected recurrence. In one case the disease was unilateral, a retinal detachment and retinal haemorrhages destroyed the sight of the irradiated eye. The remaining 9 (60 per cent.) children have attended schools and have enjoyed sufficient sight for educational needs, to see their way about and to participate in most games.

## COMMENTARY

The treatment of glioma retinae by radium is under trial, with changes in technique, and the dose is at present empirical. It seems that a dose of 3,500 r is effective in destroying this very radiosensitive neoplasm. The method of interstitial irradiation

by the insertion of a radon seed through the sclera into the substance of the neoplasm has been abandoned for that of suturing the seed, or several seeds at appropriate intervals of 7 mm. to the sclera over the site of the glioma marked out on the sclera by surface diathermy and checked by ophthalmoscopic examination. Trial is now being made with radium plaques of silver or aluminium 0·5 mm. thick containing radium salt, shaped to the radius of curvature of the sclera and secured thereto with fine silk sutures.

The results of treatment are good when the neoplasm occupies a quadrant or less of the globe and the visual result is better when the islands of glioma are at or in front of the equator. In the case of a growth at or near the macula and optic disc it is preferable, in order to avoid the dense choroido-retinal scarring which occurs immediately beneath the site where the radium is placed on the sclera and damage to the larger branches of the central retinal vessels, to place the source of radium a little remote from the growth, towards the periphery but leaving it within the range of effective irradiation.

Serious complications such as retinal detachment, large intra-ocular haemorrhages and ultimately shrinkage of the globe occur in cases where about half or more of the interior of the eye is occupied by the neoplasm and when it has been necessary to place radon seeds over the large branches of the central retinal vessels as these curve near the optic disc.

In my opinion it will be justifiable in future to treat unilateral cases of glioma by radium if the neoplasm occupies a quadrant of the globe or less. However, it is seldom that an infant is brought for examination at such a stage and generally half or more of the retina is destroyed before attention is drawn to the disease.

### MALIGNANT MELANOMA OF THE UVEAL TRACT

Stanford Cade writes "Malignant melanomata are radio-resistant tumours and their treatment by radiation is both difficult and disappointing. It is, however, unfortunate that radioresistance—a comparative term used to indicate the degree of sensitivity to radiation of one tissue as compared with another—should have been given a meaning synonymous with that of 'unsuitability for radiation'" and Ellis comments "this attitude (that melanomata are radioresistant and unsuitable for radiotherapy) moreover seems to be so universally adopted at radiotherapeutic centres in various parts of this country and America, that it would seem the time is ripe for suggesting the contrary opinion, for which there can be adduced a good deal of evidence of an incontrovertible kind, that some melanomas, at any rate, are radiosensitive."

H. Barkan commented in 1934 that the literature contained no case of malignant melanoma cured by radium. Transient regression of the neoplasm has been noted by Parker, Stokes, Janeway and Birch-Hirschfeld. Microscopic examination of excised eyes showed extensive regression but there remained small areas of well-stained and active tumour cells.

To date, the material for radiotherapy has been too small to assess the relative radiosensitivity of the various types of cell found in malignant melanomata—*e.g.*, spindle-cell (*a*) and (*b*), fascicular, endothelial, and mixed-celled neoplasms. It is evident that better results are obtained when the growth is lens-shaped, has not ruptured Bruch's membrane, and is in the vicinity of the equator. The results are appreciably less fortunate when the neoplasm involves the ciliary body and when it is adjacent to the optic disc.

Radiotherapy is justifiable in rare cases of bilateral malignant melanoma of the choroid and I think in the future this may be so for some cases of unilateral growths seen in the early stages. The following case report is an instance of a bilateral malignant melanoma of the choroid in which the neoplasm in the second eye has remained inactive 9 years after irradiation.

E.H., aged 36 (in 1939), had his left eye excised for malignant melanoma of the choroid in April, 1939. Microscopic examination showed a pigmented spindle-celled neoplasm. In the right eye a lens-shaped greyish-brown swelling was seen on the nasal side about the equator between the 2.30 o'clock and 4 o'clock meridians. Its size was assessed as carefully as possible by ophthalmoscopic examination and at operation its limits were marked out by four surface diathermy applications to the overlying sclera and checked by the ophthalmoscope. Within this marked quadrilateral area whose sides measured 8, 5, 8 and 3 mm. respectively 3 x 2 mc. radon seeds were sewn to the sclera. The depth of the growth had been approximately assessed by the ophthalmoscope at 4 mm.

In eight weeks the neoplasm was reduced to a flat plaque and it has remained thus with no sign of activity to-date April, 1948. The vision of this eye is 6/5. There are a few vacuoles in the upper nasal quadrant of the posterior cortex of the lens but these cause no visual disturbance.

Another case of a malignant melanoma adjacent to the optic disc on the nasal side was successfully irradiated in 1940, has kept his eye to-date (1948) but some obliteration of small vessels in the optic disc caused optic atrophy to become evident 7 to 8 weeks after irradiation.

Three other cases of malignant melanoma of the choroid and one of the ciliary body have been treated by radon seeds at St. Bartholomew's Hospital. In one case in 1932 there was a mushroom-shaped malignant melanoma of the choroid which had burst through Bruch's membrane just behind the equator. The neoplasm diminished in size after irradiation with 4 radon seeds and 5 months after operation it seemed likely on ophthalmoscopic examination that some viable neoplasm was still present and so

the eye was excised. After excision the neoplasm measured 9·9 x 7 x 4 mm. The area of effective irradiation as judged by microscopic evidence of chromatolysis, necrobiosis, degenerative changes and obliteration of the blood vessels was found in serial sections to be 8·5 x 6 x 2 mm.

Another case of malignant melanoma of the choroid in an only eye was treated by 4 x 1 mc. radon seeds on October 8, 1935, the growth shrank to a flat plaque and remained so till December, 1937, when it began to grow again. The lower half of the retina became detached and the vision reduced to hand movements. It seemed justifiable to attempt local excision after reflecting a scleral flap. This was done by a combination of surface diathermy along the lines planned for the scleral flap incision and a cutting diathermy needle in the choroid around the base of the neoplasm when this was exposed. The neoplasm was removed without loss of vitreous and with no apparent damage to the retina which was seen in the wound after removal of the growth and before tying the sutures in the scleral trap-door. This was done on December 17, 1937. The post-operative course was remarkably uneventful till a vitreous haemorrhage occurred during the third week. The patient was alive and well when he was last heard of in September, 1939. He could see his way about in familiar surroundings, but could not read. He declined to attend hospital for further follow-up examinations.

In another case of malignant melanoma of the choroid the growth was markedly reduced in size, the patient died about 1½ years later of some other disease. He was a Jew and his relatives refused post-mortem examination, so a valuable specimen was lost.

One case of richly pigmented malignant melanoma of the ciliary body between 2 and 5 o'clock was treated by 3 x 2 mc. radon seeds sutured to the sclera. The neoplasm shrank in 8 weeks to half its size. Fourteen weeks after operation pain, lacrimation, conjunctival congestion and photophobia made the patient request excision of the eye.

### METASTATIC CARCINOMA OF THE CHOROID

If this occurs in an only eye or, as it rarely does, in both eyes, irradiation by radon seeds is successful and justifiable in so far that this procedure saves the eye and some measure of sight which the sufferer is able to enjoy before he dies.

I thank the following surgeons for recommending patients: Mr. Gibb, Mr. Neame, Mr. Doyne, Mr. Davenport and Mr. Rycroft (London); Mr. Stirling and Mr. MacNabb (Manchester); Mr. Holmes (Liverpool); Mr. Ashdown Carr (Derby); Mr. Gann (Peterborough); Mr. Aitchison (Newcastle-upon-Tyne); Mr. Galloway (Nottingham); and Mr. Colley (Bath).

I also thank Mr. Stewart and Mr. G. S. Innes, Radium Department, St. Bartholomew's Hospital, for valued advice.

In conclusion I express my lasting gratitude to my late chiefs. To Mr. Foster Moore for the privilege I enjoyed of assisting him in his pioneer work on this subject, for the stimulus of his clear and honest observations, and for his generosity in allowing me to treat some of his cases at St. Bartholomew's Hospital. To Sir John Parsons, that " Master " of the physiology and pathology of the eye, I owe a high example of the manner in which to seek academic truth.

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## A POINT FOR CONSIDERATION IN THE USE OF THE STEREOSCOPE

BY

FRANK W. LAW

LONDON

IT recently occurred to the writer that it would be of value to know the answer to the question " What happens to the inclination of the visual axes on moving the stereogram in a stereoscope towards or away from the observer? " The question seemed simple; the answer was not obvious. Further, enquiry in various directions discovered the somewhat consoling result that the answer was not generally known; indeed, it had not been considered by most of those asked, which is surprising, in view of the common habit of sending a patient home to " do exercises with a stereoscope."

On investigating the subject it is soon apparent that the interocular distance is a factor of fundamental importance. This can be demonstrated by considering three diagrams (Figs. 1, 2 and 3) in which the stereogram card is depicted as placed at three different distances from the lenses of the instrument. Fig. 1 shows it placed at the focal plane; the emergent pencil of light has parallel rays, and the amount of convergence is independent of the interocular distance. In Fig. 2 the card is represented as nearer than the focal plane; the emergent pencils are divergent and greater inter-

ocular distance involves greater convergence. In Fig. 3, with the card beyond the focal plane, the emergent pencils are convergent, and greater interocular distance involves less convergence. In each figure the lens combinations are represented diagramatically; the optical centres are at 0.

One may now re-consider the phenomenon depicted in the figures by studying a chart obtained by calculation. Table I shows the

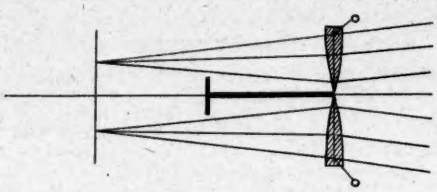

FIG. 1.

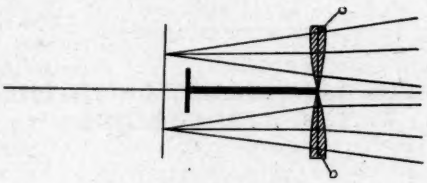

FIG. 2.

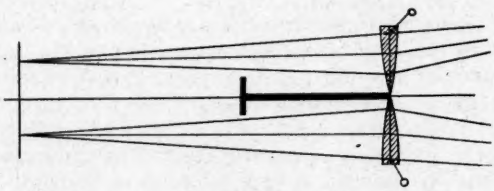

FIG. 3.

calculations for a stereoscope with lenses of +5·0D., optical centres 8·8 cms. apart, pictures separated by 5 cms. Three positions of the stereogram are considered. The fact, depicted in Fig 1, that when the card is placed at the focal plane, convergence is independent of interocular distance, emerges at once. Other interesting facts also appear; the same stereogram moved in the same direction and through the same distance induces an increase of convergence when the interocular distance is 5·2 cms., a smaller increase when it is 5·4 cms., and an actual decrease when

it is 5·8 cms. Further, with the card at 25 cms., a greater interocular distance involves a reduced degree of convergence.

Table II, calculated for a stereoscope with lenses of +4·0D., optical centres 9 cms. apart, and 5 cms. separation of the stereograms, shows lower convergence figures, but exactly the same tendencies.

TABLE I

| Width of Stereogram | Distance from Lenses | Interocular Distance | | | |
|---|---|---|---|---|---|
| | | 5·2 cm. | 5·4 cm. | 5·8 cm. | 6·2 cm. |
| | | Convergence in Prism Dioptres | | | |
| 5 cm. | 10 | 17·2 | 18·1 | 19·8 | 21·6 |
| | 20 | 19·0 | 19·0 | 19·0 | 19·0 |
| | 25 | 19·4 | 19·2 | 18·7 | 18·3 |

TABLE II

| Width of Stereogram | Distance from Lenses | Interocular Distance | | | |
|---|---|---|---|---|---|
| | | 5·2 cm. | 5·4 cm. | 5·8 cm. | 6·2 cm. |
| | | Convergence in Prism Dioptres | | | |
| 5 cm. | 11 cm. | 14·7 | 15·5 | 16·3 | 17·1 |
| | 25 | 16·0 | 16·0 | 16·0 | 16·0 |
| | 33·3 | 16·3 | 16·1 | 15·7 | 15·3 |

The practical deduction to be made from the above is that, once one has decided for what exact purpose one requires a patient to use a stereoscope, it is essential to choose an appropriate instrument and, having measured the patient's interocular distance, to calculate how the instrument will have to be used, and instruct the patient accordingly. With this in view, tables have been constructed showing the actual deviation of the visual axes involved for varying width of stereogram, and varying positions of the pictures. In Table III the basis is for lenses of 5·0D., optical centres 8·8 cms. apart; in Table IV the lenses are 4·0D. in strength, with optical centres 9 cms. apart. In each case the distance from lens to ocular centre is assumed to be 3 cms.; + (plus) indicates convergence and − (minus) divergence.

The heavy stepped line which crosses each Table is an important line of demarcation. It will be seen that the figures above this line demonstrate a common tendency—that an approach of the stereograms towards the eyes causes an increase of convergence; those below the line, that an approach of the stereograms towards

the eyes causes a decrease in convergence, or an increase in divergence.

The practical application of these Tables would be relatively simple. Having ascertained the patient's interocular distance one can see at a glance which card and which direction of movement will give the effect desired in the particular case to be treated. This will at least prevent the patient from being asked to do exercises inappropriate to his condition—and one cannot but feel that such an event must have occurred. It may, however, be considered that, when convergence or divergence is the only factor which it is desired to vary, a simpler course would be to give the patient a stereoscope with rotating prisms and place the stereograms in the focal plane.

TABLE III

| Stereogram | | Interocular Distance (cm.) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Width | Distance from Lens | 4·6 | 4·8 | 5·0 | 5·2 | 5·4 | 5·8 | 6·2 | 6·6 |
| 3 cm. | 10 cm. | + 32·2 | 33·1 | 34 | 34·9 | 35·8 | 37·6 | 39·4 | 41·2 |
| | 20 | + 29 | 29 | 29 | 29 | 29 | 29 | 29 | 29 |
| | 25 | + 28·3 | 28·1 | 27·9 | 27·7 | 27·5 | 27·1 | 26·7 | 26·3 |
| 4 cm. | 10 cm. | + 23·4 | 24·3 | 25·2 | 26·1 | 27 | 28·8 | 30·6 | 32·4 |
| | 20 | + 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |
| | 25 | + 24·1 | 23·9 | 23·7 | 23·5 | 23·3 | 22·9 | 22·5 | 22·1 |
| 5 cm. | 10 cm. | + 14·6 | 15·5 | 16·4 | 17·2 | 18·1 | 19·8 | 21·6 | 23·4 |
| | 20 | + 19 | 19 | 19 | 19 | 19 | 19 | 19 | 19 |
| | 25 | + 20 | 19·8 | 19·6 | 19·4 | 19·2 | 18·7 | 18·3 | 17·9 |
| 6 cm. | 10 cm. | + 5·8 | 6·7 | 7·6 | 8·4 | 9·3 | 11 | 12·8 | 14·6 |
| | 20 | + 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 |
| | 25 | + 15·9 | 15·7 | 15·5 | 15·3 | 15·0 | 14·6 | 14·2 | 13·8 |
| 7 cm. | 10 cm. | — 2·9 | — 2 | — 1·1 | — 0·2 | + 0·6 | + 2·3 | + 4·1 | + 5·8 |
| | 20 | + 9 | + 9 | + 9 | + 9 | + 9 | + 9 | + 9 | + 9 |
| | 25 | + 11·8 | + 11·6 | + 11·4 | + 11·2 | + 11 | + 10·5 | + 10·1 | + 9·7 |
| 8 cm. | 10 cm. | — 11·4 | — 10·5 | — 9·6 | — 8·7 | — 7·9 | — 6·2 | — 4·4 | — 2·7 |
| | 20 | + 4 | + 4 | + 4 | + 4 | + 4 | + 4 | + 4 | + 4 |
| | 25 | + 7·6 | + 7·4 | + 7·2 | + 7 | + 6·8 | + 6·4 | + 6 | + 5·6 |
| 9 cm. | 10 cm. | — 20·1 | — 19·2 | — 18·3 | — 17·4 | — 16·6 | — 14·9 | — 13·1 | — 11·3 |
| | 20 | — 1 | — 1 | — 1 | — 1 | — 1 | — 1 | — 1 | — 1 |
| | 25 | + 3·5 | + 3·3 | + 3·1 | + 2·9 | + 2·7 | + 2·3 | + 1·9 | + 1·5 |
| 10 cm. | 10 cm. | — 28·8 | — 27·9 | — 27 | — 26·1 | — 25·3 | — 23·5 | — 21·7 | — 19·9 |
| | 20 | — 6 | — 6 | — 6 | — 6 | — 6 | — 6 | — 6 | — 6 |
| | 25 | — 0·6 | — 0·8 | — 1 | — 1·2 | — 1·4 | — 1·8 | — 2·2 | — 2·6 |
| 11 cm. | 10 cm. | — 37·6 | — 36·7 | — 35·8 | — 34·9 | — 34·1 | — 32·3 | — 30·5 | — 28·7 |
| | 20 | — 11 | — 11 | — 11 | — 11 | — 11 | — 11 | — 11 | — 11 |
| | 25 | — 4·8 | — 5 | — 5·2 | — 5·4 | — 5·6 | — 6 | — 6·4 | — 6·9 |

TABLE IV

| Stereogram | | Interocular Distance (cm.) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Width | Distance from Lens | 4·6 | 4·8 | 5·0 | 5·2 | 5·4 | 5·8 | 6·2 | 6·6 |
| 3 cm. | 11 cm. | + 27·6 | 28·5 | 29·4 | 30·3 | 31·1 | 32·9 | 34·7 | 36·4 |
| | 25 | + 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |
| | 33·3 | + 23·1 | 22·9 | 22·7 | 22·5 | 22·3 | 21·9 | 21·5 | 21·1 |
| 4 cm. | 11 cm. | + 19·8 | 20·7 | 21·6 | 22·5 | 23·3 | 25·1 | 26·9 | 28·6 |
| | 25 | + 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| | 33·3 | + 20 | 19·8 | 19·6 | 19·4 | 19·2 | 18·8 | 18·4 | 18 |
| 5 cm. | 11 cm. | + 12 | 12·9 | 13·8 | 14·7 | 15·5 | 16·3 | 17·1 | 20·8 |
| | 25 | + 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 33.3 | + 16·9 | 16·7 | 16·5 | 16·3 | 16·1 | 15·7 | 15·3 | 14·9 |
| 6 cm. | 11 cm. | + 4·2 | 5·1 | 5·9 | 6·8 | 7·7 | 9·4 | 11·2 | 13 |
| | 25 | + 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | 33·3 | + 13·8 | 13·6 | 13·4 | 13·2 | 13 | 12·6 | 12·2 | 11·8 |
| 7 cm. | 11 cm. | — 3·6 | — 2·7 | — 1·9 | — 1 | — 0·1 | + 1·6 | + 3·4 | + 5·2 |
| | 25 | + 8 | + 8 | + 8 | + 8 | + 8 | + 8 | + 8 | + 8 |
| | 33·3 | + 10·7 | + 10·5 | + 10·3 | + 10·1 | + 9·9 | + 9·5 | + 9·1 | + 8·7 |
| 8 cm. | 11 cm. | — 11·4 | — 10·5 | — 9·6 | — 8·8 | — 7·9 | — 6·2 | — 4·4 | — 2·6 |
| | 25 | + 4 | + 4 | + 8 | + 4 | + 4 | + 4 | + 4 | + 4 |
| | 33·3 | + 7·6 | + 7·4 | + 7·2 | + 7 | + 6·8 | + 6·4 | + 6 | + 5·6 |
| 9 cm. | 11 cm. | — 19·2 | — 18·3 | — 17·4 | — 16·6 | — 15·7 | — 14 | — 12·2 | — 10·4 |
| | 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 33·3 | + 4·5 | + 4·3 | + 4·1 | + 3·9 | + 3·7 | + 3·3 | + 2·9 | + 2·5 |
| 10 cm. | 11 cm. | — 27 | — 26·1 | — 25·2 | — 24·4 | — 23·5 | — 21·8 | — 20 | — 18·3 |
| | 25 | — 4 | — 4 | — 4 | — 4 | — 4 | — 4 | — 4 | — 4 |
| | 33·3 | + 1·4 | + 1·2 | + 1 | + 0·8 | + 0·6 | + 0·2 | — 0·2 | — 0·6 |
| 11 cm. | 11 cm. | — 34·8 | — 33·9 | 33 | 32·3 | 31·3 | 29·6 | 27·8 | 26·1 |
| | 25 | — 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| | 33·3 | — 1·7 | 1·9 | 2·1 | 2·3 | 2·5 | 2·6 | 3·3 | 3·7 |

If, however, accommodation is also to be varied, the simpler stereoscope is more effective—again provided that one is fully aware of how it should be used; and this brings one to the interesting consideration of the relationship, when using a stereoscope, between accommodation and convergence. In this connection a Table has been calculated showing the position of any card at which accommodation balances convergence. The range over which this can obtain is limited. Cards separated by a distance of less than 4 cms. cannot be brought sufficiently close to the lenses to induce the required amount of accommodation. On the other hand, beyond the focal plane accommodation is absent

or negative, and cards separated by more than 10 cms. require divergence in all positions for superimposition to occur. Within the remaining range, however, the convergence can be calculated from the figures in Tables III and IV and expressed in metre-angles by dividing the figure representing prism dioptres of convergence by the interocular distance in cms. Thus, taking the first item in Table III, $\frac{32{\cdot}2}{4.6} = 7$ M.A. The results are shown in Table V, and are of interest in demonstrating the wide fluctuations in the accommodation factor induced by movement of the stereograms. The Table enables one to apply an exercise for

TABLE V

| Stereogram Width | 5 OD. LENSES | | 4 OD. LENSES | |
|---|---|---|---|---|
| | Distance from Lens | Acc (D) = Conv (M.A.) | Distance from Lens | Acc (D) = Conv (M.A.) |
| 4 cms. | 9·5 | 4·5 | 11·7 | 4·4 |
| 5 cms. | 11·4 | 3·4 | 15 | 2·9 |
| 6 cms. | 13·8 | 2 2 | 18 | 1·9 |
| 7 cms. | 16·4 | 1·2 | 20·2 | 1·1 |
| 8 cms. | 18·5 | 0·5 | 22·8 | 0 5 |
| 9 cms. | 20 | 0 | 25 | 0 |

improving accommodation and convergence together with scientific accuracy; the bar of the stereoscope could with advantage be marked to indicate the accommodative effort demanded.

It is a pleasure to express my grateful thanks for the courteous and enthusiastic collaboration of Mr. S. P. Holloway in the preparation of this article, and for his drawing up of the Tables.

# THE EFFECT OF AGE AND ILLUMINATION UPON VISUAL PERFORMANCE WITH CLOSE SIGHTS

BY

H. C. WESTON

## 1. INTRODUCTION

THIS paper is based upon the results of an experimental investigation, in which twelve subjects performed a series of special visual tasks involving the perception of fairly small detail. Each task in the series was performed at each of six values of illumination which were so chosen as to form a geometric series. The lowest value was 0·5 lumen per square foot (*i.e.*, 0·5 foot-candle), and the highest was approximately 500 $1m/ft^2$, so that the range covered all values likely to be used in practice for comparable tasks done either with natural or artificial lighting. The brightness of the visible environment (panoramic brightness) was varied *pari passu* with that of the local field of attention, so as to maintain a ratio of the former to the latter of not less than 0·5.

As it was not the object of the experiments to obtain data relating to the variation of visual performance with age, the subjects were not chosen accordingly. Subsequently, however, it was found that they were distributed by age in five consecutive quinquenniads covering, approximately, the middle third of life. Hence, the data obtained relate to five small groups, in three of which there were two subjects, while in each of the other two groups there were three subjects. An unusual and, for the present purpose, a very fortunate circumstance, is that similar visual performance tests were done under similar illuminations by the same subjects at times separated by an interval of five years. So, it is possible not only to compare the performances of the five different age groups, but also to show the effect of a five year difference of age upon the performance of each group.

## 2. REFRACTION AND ACUITY OF SUBJECTS

All the subjects are experienced observers, being members of the scientific staff of the National Physical Laboratory. Prior to the second series of experiments, they were examined by Mr. Graeme Talbot, F.R.C.S., and new glasses were prescribed as required (see Table I).

All the subjects read J.I. with their glasses. One is a fairly high myope, but the others are only slightly ametropic. Group

acuity does not appear to be related to group age and, in fact, the clinical findings show no important difference of acuity among the group.

| Age Group at Date of refraction | Subject | R. eye | L. eye | Phoria at near |
|---|---|---|---|---|
| 24-28 | 1 | $\frac{-0{\cdot}25}{-0{\cdot}25\,175^\circ}$ = 6/5 | $\frac{-0{\cdot}25}{-0{\cdot}50\,170^\circ}$ = 6/5 | 0 |
| | 2 | $\frac{-2{\cdot}5}{-0{\cdot}5\,50^\circ}$ = 6/6 | $\frac{-2{\cdot}5}{-0{\cdot}5\,30^\circ}$ = 6/6 | 4 ESO |
| 29-33 | 3 | $\frac{-0{\cdot}5}{+0{\cdot}50\,95^\circ}$ = 6/6 | $\frac{-0{\cdot}5}{+0{\cdot}75\,60^\circ}$ = 6/12 | 3 ESO |
| | 4 | $\frac{0}{+0{\cdot}25\,95^\circ}$ = 6/6 | $\frac{0}{+0{\cdot}25\,80^\circ}$ = 6/6 | 0 |
| | 5 | $\frac{0}{-2{\cdot}50\,10^\circ}$ | $\frac{-0{\cdot}25}{-1{\cdot}75\,173^\circ}$ | 0 |
| 34-38 | 6 | $\frac{-1{\cdot}25}{-0{\cdot}50\,160^\circ}$ = 6/5 | $\frac{-1{\cdot}0}{-0{\cdot}5\,55^\circ}$ = 6/5 | 4 ESO |
| | 7 | $\frac{+3{\cdot}0}{+0{\cdot}75\,83^\circ}$ = 6/5 | $\frac{+0{\cdot}25}{-}$ = 6/5 | 2 EXO |
| 39-43 | 8 | $\frac{-0{\cdot}25}{+1{\cdot}0\,105^\circ}$ = 6/5 NEAR ADD. | $\frac{-}{+0{\cdot}5\,90^\circ}$ = 6/5 $+0{\cdot}5$ | 4 EXO |
| | 9 | $\frac{-}{+0{\cdot}5\,10^\circ}$ = 6/6 NEAR ADD. | $\frac{-0{\cdot}25}{+0{\cdot}5\,145^\circ}$ = 6/6 $+0{\cdot}25$ | 0 |
| | 10 | $\frac{-1{\cdot}0}{-0{\cdot}5\,70^\circ}$ = 6/6 | $\frac{-1{\cdot}25}{-0{\cdot}25\,35^\circ}$ = 6/6 | 0 |
| 44-48 | 11 | $\frac{-0{\cdot}25}{+0{\cdot}5\,25^\circ}$ = 6/5 NEAR ADD. | $\frac{-0{\cdot}25}{+0{\cdot}50\,110^\circ}$ = 6/6 $+1{\cdot}25$ | 4 EXO |
| | 12 | $\frac{-9{\cdot}5}{-1{\cdot}0\,105^\circ}$ = 6/6 NEAR ADD. | $\frac{-12{\cdot}5}{-0{\cdot}5\,10^\circ}$ = 6/9 $+2{\cdot}0$ | 16 EXO |

### 3. MEASUREMENT OF VISUAL PERFORMANCE

In this paper *visual performance* means the *rate* of accomplishing a specific visual task, *e.g.*, the discrimination of visual objects having a prescribed characteristic, when these objects are presented along with others in an objective field of sight whose angular size is typical of " near work." The test-objects employed were Landolt rings, arranged as shown in Fig. 1. The rings differ only in the orientation of the gap, eight positions of the latter being used. The visual task consisted in finding all the rings

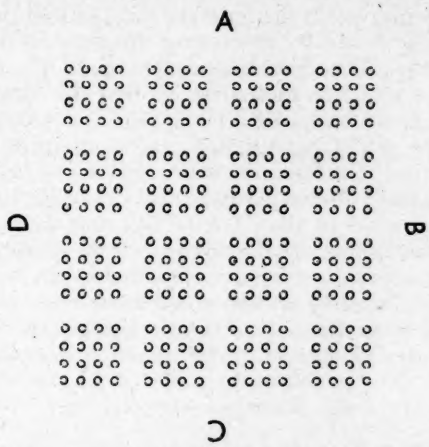


FIG. 1.

having the gap in one prescribed position, and so it involved some scrutiny of every ring present in " the sight." The severity of the visual task was varied by using three sizes of ring, such that, at ordinary reading distance, the visual angles subtended by the gaps were, respectively, 1·5, 3 and 4·5 minutes of arc. Of these sizes, the intermediate one corresponds approximately to the size of detail in the news columns of the daily press.

These visual tasks may be compared with practical tasks such as proof-reading, reading numerals, and many inspection tasks done in factories, offices, schools, etc. Clearly the rate of performance can only be ascertained by measuring the time taken by viewer to complete the task. But, as some reaction is necessary for the purpose of indicating that the objects of search have been recognized, the total time taken to deal with each test sight must include this reaction or motor response time. The two components of the time per test, that is, the visual discrimination time and the

indicator action time, cannot be separately measured; hence, an exact determination of the discrimination time is impossible, though, by a suitable technique, it can be ascertained to a fairly close approximation. In these tests the method adopted was as follows. The subjects were asked to indicate the prescribed rings by cancelling them with a stroke of the pencil. They were first given a test sheet on which all the prescribed rings were made extremely conspicuous by being filled in with red ink, thus converting them to red spots. By this means the search time was minimised, the time taken by the subject to work through the test material being almost entirely time occupied in manual action. The test was then given in the ordinary way, so that the prescribed objects had to be found by discerning the gaps in the rings and their orientation. The time required to work through the test material in this way was measured, so that the time per correct ring cancelled could be found. From this was deducted the time required for the act of cancellation, as found from the red-spot test. The net time thus obtained is the closest practicable approximation to the actual discrimination time. This has been corrected when necessary, so as to allow for the fact that the subjects sometimes overlooked some of the rings which should have been cancelled, that is to say, it has been divided by an accuracy factor so as to obtain the time which would have been required for a perfectly accurate performance. The reciprocal of this corrected value is the index of speed of discrimination used in this paper.

### 4. Results Obtained

The individual performance values obtained at each illumination, and with each visual task, have been averaged for each age group. From these averages graphs were prepared showing the variation of performance with illumination. As would be expected, owing to the small number of observations available for each age group at any one illumination and size of test-object, all the points plotted did not lie upon smooth curves. Allowing, however, for unmistakably exceptional results, smooth curves were fitted to the plots, and the performance values derived from these curves are those which have been used in preparing Figs. 2, 3, and 4. In this connection it should be said that the smoothing of the actual observations, while it removes irregularities which are unlikely to have appeared had more data been available for analysis, does not effect the main conclusions to be drawn from these experiments; that is to say, the invariable decline of visual performance with age which is exhibited by the diagrams is found also, and on the average to the same extent, by comparison of the raw data.

Referring now to Fig 2, it can be seen that the points plotted

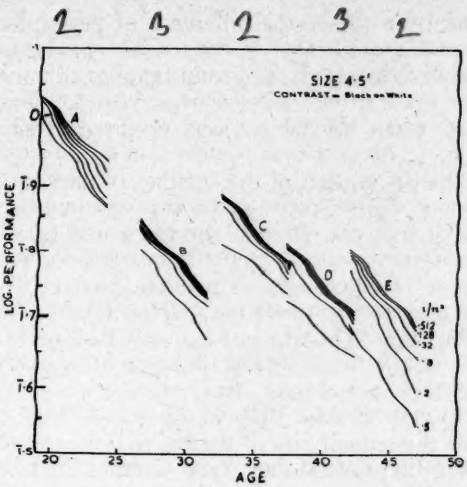


FIG. 2.

refer to ages ranging from 19 to 47 years, and to the logarithms of the value of visual performance. By plotting log. performance all the results are shown on a relative basis, that is to say, the difference on the vertical scale between any two values, is proportional to the *ratio* of those values, and this ratio can readily be found, if desired, from tables of antilogarithms. For example, the scalar difference between the value plotted for group E at 32 lm/ft² and age 47 years, and that plotted for group A at the same illumination and age 24 years is 0·23, which means that E's performance is only equal to 59 per cent. of A's. Similarly, it can be found that A's performance at 0·5 lm/ft² and age 24, is about equal to 85 per cent. of the performance achieved by the same group at the same age when the illumination was increased to 500 lm/ft².

In Fig. 2 all the lines joining pairs of points have a downward slope, so that it is clear that an advance in age of 5 years is accompanied by a decline in performance in the case of each group, and with all the values of illumination. Consistent with this finding is the obvious decline from group to group as the group-age advances. The general trend of the results might be shown by drawing a straight line across the diagram in such a way that approximately an equal number of all the points plotted lies above and below the line. If this were done it would be found that the downward slope of this line is less steep than that of the lines drawn for each separate age group, so that the annual rate of decline which might be estimated in this way would be lower than

the rate found from the 5-year difference of performance actually observed for each group. One reason for this apparent discrepancy is that the relative levels of the group families of curves certainly depend partly upon group differences of visual ability which, no doubt, existed when all the subjects of these experiments were of the same age. As to this, it is clear that no direct evidence can be had, but the disposition of the families of curves, and particularly the obvious displacement of the B group family, leaves little room for doubt that the different groups would have been found unequal in efficiency could their performance have been measured when they were of equal age. Thus, the decline in performance from one age group to next does not indicate the true rate of decline with advancing age. The true rate can only be found from chronologically different performances of the same individuals or groups, such as are here presented. But, since these chronologically different performances refer only to a 5-year change of age, they do not enable the annual rate of decline to be found for the whole middle third of life, nor do they show whether the rate is constant or variable during this period. On these points, however, the results shown in Fig. 2 are suggestive. It can be seen that, except at the lower values of illumination, the slope of the curves is much the same for each age group, and so, for the particular visual task considered, it would appear that the rate of decline does not vary much from year to year, though it tends to increase during the last quinquennium, *i.e.*, between the ages of 42 and 47. On the average, it is of the order of 5 per cent. per annum with moderate to high values of illumination.

The illumination relating to each performance curve is shown in Fig. 2. It is evident that varying the illumination of the test material has a more marked effect upon visual performance as age advances and, in the case of group E, the spread of the family of curves is twice as wide as it is for group A. It may be noted that, at the age of 45, the performance achieved with an illumination of 500 lm/ft$^2$ is not as good as that achieved at the age of 25 years, with an illumination of only 0·5 lm/ft$^2$. Moreover, after the lapse of 5 years, no group gives the same performance at the highest illumination as it formerly did at the lowest illumination. Although this result is surprising, and is not consistent with the results obtained with smaller test-objects, it seems clear that any considerable advance in age cannot be fully compensated by any reasonable adjustment of the illumination level for visual tasks of this kind.

Turning now to Fig. 3, it will be seen that the decline from group to group is somewhat steeper than it is with the larger test-object dealt with in Fig. 2. But the annual rate of decline, as indicated by the different families of curves, is much the same. Here, however, in the case of the older subjects—groups C, D,

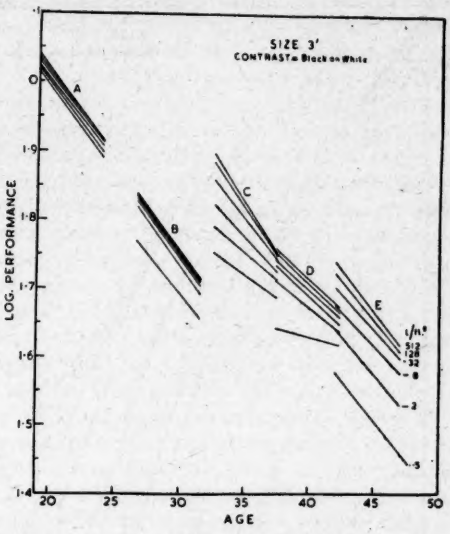


FIG. 3.

and E—an illumination of 8 $1m/ft^2$ gives a performance similar to that achieved 5 years earlier by the same subjects with an illumination of 0·5 $1m/ft^2$; while 500 $1m/ft^2$ gives a performance similar to that formerly given by 2 $1m/ft^2$, though, again, it is evident that high illumination does not fully compensate for any considerable advance in age.

Fig. 4 shows the results obtained for the most difficult visual task. As might be expected, the greatest decline from group to group is here exhibited, and the average annual rate of decline throughout the age span considered is more than 7 per cent. The spread of the families of curves relating to age groups B, C, D, and E is much wider than is the case with the easier visual tasks, thus showing that the performance of all the subjects in these age groups, *i.e.*, those whose age is 25 years or more, is much affected by the level of illumination, particularly when this falls below about 30 $1m/ft^2$. Actually, a change from the lowest to the highest illumination tried increases the performance of the youngest subjects only by 18 per cent., but it increases the performance of the oldest subjects fourfold. It is also of interest to note that, with the lowest illumination and the finest visual task, the performance of subjects aged 24 years is just as good as that of subjects aged 47 years with the easiest visual task, and the highest illumination (compare Figs. 2 and 4).

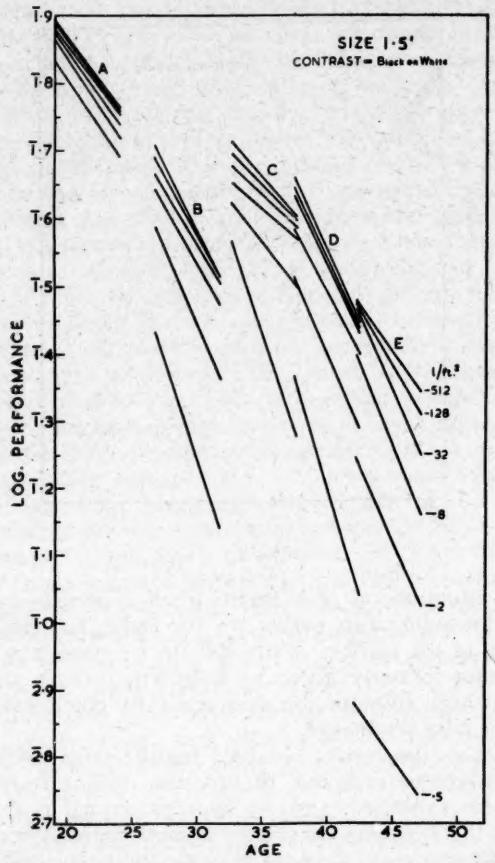


FIG. 4.

## 5. CONCLUSION

It should be clearly understood that the decline shown by the results of the experiments discussed does not refer to the resolving power of the eyes, but to the quickness of perception, that is, to a function of vision which is not evaluated by clinical tests. Even so, the extent of the decline, and its early onset, may seem surprising, and perhaps depressing. It must be remembered, however, that most everyday visual tasks do not involve continuous scrutiny of small detail, and so the performance of them will not generally be so much affected in the advance to " middle-age "

as is the performance of the visual tasks considered in this paper. Nevertheless, visual efficiency appears to come to its maximum in early adulthood, and, thereafter, to fall off at a greater rate than we realise. This is in keeping with other findings concerning ageing. For example, Bouma[1] has shown that contrast sensitivity is a function of age, and that it diminishes from the mid-twenties onwards; Mann and Sharpley[2] have found there is a tendency for the rod field of the dark-adapted eye to contract with advancing age, this tendency becoming apparent at about the age of 30 years; and it has been shown that manual motility begins to decline in the late twenties[3]. Probably many accidents should be attributed to the slowing down of vision as age advances, and it is well known that dissatisfaction with standards of artificial lighting commonly found in workplaces is most prevalent among middle-aged and elderly workers. The general tendency for visual performance to decline from a fairly early age, which, in spite of the few subjects studied, is so consistently shown by the results presented in this paper, is certainly subject to individual exceptions. Indeed, individually, some of the subjects of these experiments showed different rates of decline, and probably began their decline at different, though not widely different, ages.

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## SIDELIGHTS ON THE INFERIOR OBLIQUE MUSCLE

BY

J. RINGLAND ANDERSON

MELBOURNE

### ANATOMICAL FEATURES

The relationships of this muscle to the inferior rectus and to the capsule of Tenon and neighbouring orbital fascia require emphasis. These are assuming greater importance as the inferior oblique muscle is directly or indirectly concerned with an increasing number of surgical procedures. The connection between the sheaths of the two inferior muscles and Tenon's capsule restricts the effect of division of the inferior oblique muscle. The results of such an operation may vary with the intimacy of such connections and the strength of the check ligaments.

" English anatomists do not appear to have paid minute attention to this subject." So wrote Lockwood in 1886, 83 years after Tenon's discovery of the capsule that bears his name. If attention has been paid to it since, a perusal of the literature does not make a clear conception obvious. The following description based largely on dissections of refrigerated foetal material appears to the author as accurate (fig. 1).

Tenon's capsule is the membrane surrounding the globe from the limbus to the optic nerve. It varies in thickness, being thickest

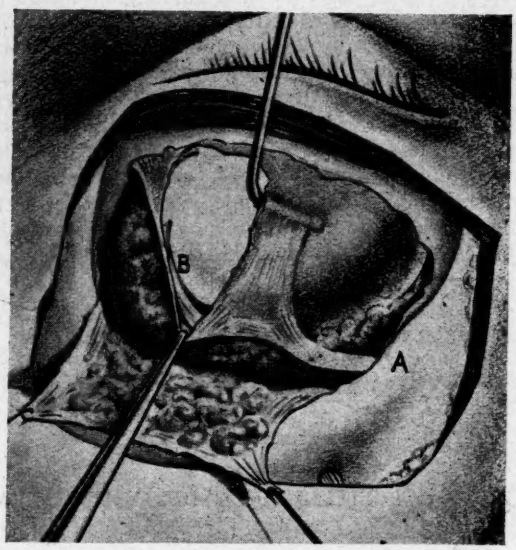


FIG. 1.

The septum orbitale has been opened, a portion of it is seen above, but it is mostly turned down over the zygomatic margin of the right orbit. Over this lies the superficial layer of fat. A portion of Tenon's capsule—the intermembranous membrane between the inferior and external recti—has been excised exposing margins of these muscles and the insertion of the inferior oblique. The latter is uncovered as forceps draw downwards the suspensory ligament, with which is united the sheath of this muscle. Traction on this sheath shows its union with that of the inferior rectus.

The suspensory ligament is shown approaching its medial and lateral bony attachments. As it approaches the tubercle of Whitnall laterally, it is fused with the septum orbitale, the check ligament of the external rectus and the lateral palpebral ligament. The site for reattachment of the origin of the muscle in Wheeler's operation of advancement is marked by A. That for reattachment of the insertion in White's operation of recession is shown at B.

between the equator and the insertions of the muscles. In this area it is loosely attached to the globe by strands of episcleral tissue. In front it is firmly attached.

Each extra-ocular muscle is surrounded by a fine fibrous sheath. In front of the equator the sheaths of adjacent muscles extend towards each other, meet and fuse. These fused extensions form the inter-muscular membrane which encircles the globe in front of the equator. It is reinforced by overlying fibrous tissue.

The sheaths of the inferior muscles unite as they cross at right angles. They and the intermuscular membrane on each side are reinforced as it runs to join the medial and check ligaments at their insertions to the lacrimal and malar bones respectively. This reinforced portion was first described by Lockwood (1886), and is known as the suspensory ligament. The check ligament of the inferior rectus runs forward as a thin layer to the lower eyelid where it is attached between the tarsus and the overlying orbicularis oculi. The sheath of the inferior oblique, or according to Russell, 1948, its inferior layer, is continuous with the suspensory ligament as it runs up to its lateral attachment to Whitnall's tubercle on the zygoma. From the sheath of the inferior oblique a delicate strand of fibrous tissue runs laterally to be attached to the periorbita near the orbital floor. This, as Whitnall suggested, may be inconstant.

### Approach to Origin of the Inferior Oblique Muscle

The origin is adjacent to or rarely more than 5 millimetres from the incisura lacrimalis. The muscle passes laterally and slightly backwards between the inferior rectus and a layer of fat lying on the orbital floor.

One divides the orbicularis oculi and underlying septum orbitale down to the inferior medial border of the orbital margin where it runs obliquely upwards towards the lacrimal sac. If one inserts a muscle hook along the floor of the orbit, turns its point upwards, one engages the muscle and can draw it forwards. It may be necessary to separate it from fat for this ubiquitous packing lies on both its deep and superficial aspects. A myomectomy is performed by holding the muscle in artery forceps and removing the held portion by cutting on each side of the forceps.

As the inferior oblique muscle leaves its point of origin it is clad with a delicate sheath. It appears as if this muscle becomes attached by its sheath to the suspensory ligament, then runs below the inferior rectus and finally passes obliquely through Tenon's capsule into the space beneath it. This part of the capsule is the portion of the intermuscular membrane that joins the sheath of the external rectus along its lower border. Here the inferior oblique

muscle lies posterior to the suspensory ligament. The insertion into the sclera is oblique and about 10 millimetres in length, and lies in and below the horizontal meridian. It is under the external rectus, its anterior end being 2 millimetres above the lower level of the external rectus and almost 10 millimetres behind the insertion of this muscle. Fink, 1947. A subcapsular potential space surrounds the terminal portion of the inferior oblique muscle.

### APPROACH TO INSERTION OF THE INFERIOR OBLIQUE MUSCLE

As the insertion extends to a point usually 4 millimetres from the fovea the first essential is to rotate the eyeball well upwards and inwards. It may be kept there by a scleral suture. After incision of the conjunctiva one may engage the short tendon below the external rectus before or, more simply, after division of this muscle.

Salzmann, quoted by Whitnall and Fuchs, quoted by Berens, 1943, stated that the line of insertion often showed gross irregularities, yet Howe, quoted by Krewson (1944), found its site almost constant. Fink, 1947, found insertional variations of the inferior oblique muscle to be second only to those of the superior oblique muscle. In one of his specimens the insertion surrounded the optic nerve. The sheath of the muscle sends extensions that usually join the sheath of the nerve and surround the posterior ciliary nerve and vessels.

### FUNCTIONS OF THE INFERIOR OBLIQUE MUSCLE.

Though in opposition to Whitnall, Wolff and others it is reasonable to consider the primary action of the oblique muscles to be torsion rather than elevation or depression. This idea was stated by Maddox and Peters and has recently been clarified by Adler (1946). He considered that this muscle was 56·1 per cent. an extorter and 42·9 per cent. an elevator. It is of interest to recall the term "circumagentes" which was applied by anatomists to the oblique muscles up to the beginning of the 18th Century. Thomas Gibson in the 1688 edition of his "The Anatomy of Human Bodies Epitomized" wrote "The oblique muscles are called circumagentes, winders or rollers about, and amatorii, or amorous, and are in number two." John Brown in 1681 wrote, "These two muscles are called amatorii or the lover's muscles, being as the true messengers of affection, by some they are called circumactores or the rowling muscles, for they do much work in human body." Bartholin in 1655 and Porterfield in 1759 appeared to share this view, whilst Zinn in 1755 stated that their action was rotatory, but he used the modern titles. Dr. Kenneth F. Russell, who supplied me with this historical information, wrote "If you study a patient with a vertical coloboma when he fixes

his gaze on some distant object and then slowly move his head laterally—it will be noted that the coloboma will remain in the vertical plane for an appreciable period after the lateral movement has commenced. This amounts to about 5-7° and represents the rotation of the globe of the eye by the oblique muscles." See also Russell 1932. If we are correct in this view then there is a pair of muscles which primarily rotates vertically, horizontally and circularly or clockwise, respectively.

Though the majority of observers class the inferior oblique muscle as an abductor, Krewson (1944) recently drew attention to Volkmann's measurements which suggested that it was an adductor. He found that the muscle passed anterior to the vertical axis. The muscle is certainly in this position when the globe is rotated inwards. The diplopia in paralysis would be crossed in the extreme contralateral field if this were so.

The oblique muscles are certainly of less importance than the vertical recti in the vertical plane. The superior rectus is 73·7 per cent. effective as an elevator and the inferior oblique muscle, but 42·9 per cent.

As is well known the inferior oblique muscles, when the eyeball is in adduction, are frequently found to act in excess as elevators. This may be due to a variety of causes.

### Overaction of the Inferior Oblique Muscle

*Causes.* These have been discussed in detail elsewhere (Anderson, 1942). Here it is sufficient to classify possible causes as follows:—

(1). Primary overaction due to either asymmetry in the balance or in the insertions of the superior and the corresponding inferior oblique muscles, or to deficient fascial check ligaments or to an oblique insertion of the internal rectus. The presence of an accessory inferior oblique muscle (Whitnall) may explain overaction. Possibly excessive adhesions between the inferior oblique and the inferior or external rectus may act similarly. Chavasse appeared to consider this apparent imbalance in adduction between the oblique muscles to be the rule. It is wise, therefore, to compare the features of these two muscles. See Table 1.

Reference to this comparison shows that the superior has less vertical purchase than the inferior oblique muscle, because its tendon makes an angle that is 4½ degrees greater with the median plane than does the inferior oblique muscle. Berens (1936) quoted Verrijp who claimed that the inferior contributed more of its energy to elevation than does the superior oblique to depression as 42 per cent. is to 37 per cent.

TABLE I

| Muscle | Nerve Supply | Action, Main and Subsidiary | Length of Muscle and Tendon | Check Ligament Attachment | Origin | Insertions which are Variable | Arc of Scleral Contact | Plane of Action | Energy used in Vertical Rotation | Paralysis |
|---|---|---|---|---|---|---|---|---|---|---|
| SUPERIOR OBLIQUE MUSCLE<br><br>Origin 2nd Somite | IV | Intorsion, Abduction, Depression. | Both longest | Close to vertical meridan, attached to superior rectus | Posterior | Posterior at 45° to transverse axis<br><br>Within 7·5 mm. of optic nerve | Very small | 55° 21′ from median plane | 37% | 2nd most frequent |
| INFERIOR OBLIQUE MUSCLE<br><br>Origin 3rd Somite | III | Extorsion, Abduction, Elevation. | Shortest muscle though longer than "effective" part of S.O. No real tendon | Attached to inferior rectus and to orbital margin | Anterior even to pulley of S.O. | In horizontal meridian at 25° to line of S.O. insertion. Within 4·0 mm. of optic nerve | Large | 50° 57′ from median plane | 42% | Rarest, may be associated with internal paralysis |

(2). Overaction secondary to paresis of the homolateral superior oblique or the contralateral superior rectus. Overaction is particularly likely to occur in the former condition if the paretic eye is used for fixation. Verhoeff (1941) considered that overaction was always due to paresis of the superior oblique muscle or to hypoplasia of the trochlear nucleus.

There are two schools of thought each based on a difference in method of diagnosis. Each school blamed a different superior muscle paresis as the common cause of overaction. White and Brown (1939) following Duane found weakness of the superior rectus 28 times more frequently than that of the superior oblique muscle. Bielschowsky and his followers believed that paresis of the superior oblique was the most frequent ocular palsy.

The overaction is due, on the one hand, to lack of opposition from the paretic antagonist, the superior oblique muscle, and on the other hand to excessive stimulation following paresis of the yoke muscle, the opposite superior rectus. As Adler (1946) pointed out, part of the disagreement is due to some authors considering only primary paresis (*e.g.*, Davis, 1944), while others paresis associated with horizontal strabismus as well (White and Brown). Adler found that an isolated primary vertical palsy as studied by Davis (1944) was more commonly of the superior oblique muscle, but that the vast majority of vertical palsies associated with strabismus, as studied by White and Brown, was probably due to a weakness of the superior recti.

In my first series of 127 vertical ocular palsies accompanied by horizontal strabismus the superior rectus appeared to be at fault in 56 per cent. and the superior oblique muscle in 33 per cent. of cases. In my second series of 54 vertical ocular palsies the superior rectus was affected in 48 per cent. and the superior oblique muscle in 27 per cent. when accompanied by horizontal

TABLE II

| PARALYSIS | — Sup. R. | — Sup. O. | — Inf. R. | — Inf. O. | TOTAL | |
|---|---|---|---|---|---|---|
| With horizontal strabismus | 56% | 33% | 7% | 4% | 82 | 1st Series |
| | 48 | 27 | 18 | 6 | 33 | 2nd Series |
| Isolated vertical squint | 70 | 27 | 2 | 2 | 45 | 1st Series |
| | 57 | 33 | 5 | 5 | 21 | 2nd Series |

NOTE. In addition there were 16 cases in which the inferior rectus and the contralateral inferior oblique were affected and diagnosis of the initial lesion was not made.

TABLE III

| DISORDER | MUSCLE DEFECTS | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | +Inf. O. | | | | —Inf. O. | | | — Inf. R | —R&L Inf. O and —R&L Inf. R | — S.R | | | — S.O | | |
| | No H.D. | R | L | R&L | R | L | With —Inf. R | | | R | L | R&L | R | L | R&L |
| ALT. C.C.S. | 2 | 4 | 2 | 3 | — | — | 1 | -- | — | 1 | — | — | — | — | — |
| Right C.C.S. | 19 | 11 | 2 | 8 | — | 1 | 3 | 2 | — | 4 | — | — | 1 | 3 | — |
| Left C.C.S. | 31 | 10 | 16 | 11 | — | 1 | 2 | 1 | 1 | 1 | 4 | 2 | — | 4 | 1 |
| DIVERGENCE | 7 | 6 | 4 | 1 | — | — | 2 | 3 | 2 | 1 | 6 | — | — | 1 | — |
| Isolated Vertical Squint | — | — | — | — | — | 1 | — | 1 | 1 | 3 | 8 | — | 3 | 4 | — |
| TOTAL | 59 | 31 | 24 | 23 | — | 3 | 8 | 7 | 4 | 10 | 18 | 2 | 4 | 12 | 1 |

Eight cases of paralysis of a lateral rectus and five of true or approximately true hyperphoria were included. Fifteen doubtful cases were excluded.

GRAND TOTAL 219 cases with horizontal or vertical strabismus, paretic and so-called concomitant.
67 cases or 30% had no vertical defect.
78 cases or 36% showed an overaction of one or both inferior oblique muscles that was the only vertical defect.

In 47 cases or 22% the overaction appeared to be secondary to another vertical defect. Three times this was bilateral and associated with palsy of both superior recti and once with bilateral trochlear palsy.

In 3 cases inferior oblique palsy was unilateral, in 8 cases it was associated with weakness of the opposite inferior rectus and the initial palsy was in doubt.

In 4 cases this condition was bilateral and in 7 cases the inferior rectus was paresed.

strabismus. As isolated palsies the superior rectus was affected in 57 per cent. and the superior oblique in 33 per cent. See Tables II and III.

### RECOGNITION OF OVERACTION.

The overaction may be of the first degree, that is present on ordinary adduction, or of the second degree, present only on forced adduction or of the third degree, that is present only when the eye is looking upwards as well as inwards.

Vertical errors in ocular alignment are not easy to recognise if slight, or if associated with high degrees of convergence or divergence. Reliance on features that may be used for reference such as margins of lids and the distance from them to the pupils may be misleading. The lids may be asymmetrical. A palpebral aperture updrawn laterally below an abducted eye or down-drawn medially below an adducted eye may suggest elevation of the

FIG. 2.

An apparent right hypotropia due to the lower level of the right orbit. The true angle was 7 dioptres of right hypertropia. The cause was probably a paresis of the left inferior oblique.

adducted eye. So often facial asymmetry if not congenital soon appears as a testimony to the strain of life. The cover test is always the safest guide. One eye or even the orbit may be at a different level, and unless recognised may lead to faulty diagnosis

FIG. 3.

FIG. 4.

Retraction syndrome showing elevation excess on attempting adduction of left eye.

and surgical bewilderment. This was so in the following case :— Dorothy A. showed - LIO, - RIR, +RSR, +LSO, by the screen test and the torticollis present suggested that the original lesion was paresis of the left inferior oblique muscle. Prior to this test, however, it was considered that there was a right hypotropia. This was due to the right eye and orbit being on a lower level than the left. There were really 7 dioptres of right hypertropia at a resting angle of -2. See Fig. 2.

Faulty diagnosis was the main reason why eight separate operations were necessary in a patient reported in a recent copy of the American Journal of Ophthalmology.

The excessive elevation on attempted adduction in the retraction syndrome is still a mystery. Figs. 3 and 4 are of a boy with absent adduction and abduction and a slight left hypertropia (3). On attempting adduction the left cornea disappeared under the lid (4). Myomectomy of the inferior oblique was performed twice and the superior rectus was receded without reduction of the elevation excess.

## TREATMENT.

" A single oblique overaction if strong often necessitates an operation to weaken the muscle. The double oblique overaction can often be ignored provided that it does not interfere with the patient's binocular vision." Sheila Mayou, 1947.

(1). Tenotomy or myomectomy near the origin has been the most common operation. The approach may be cutaneous or conjunctival. It is simple to perform but has certain disadvantages. (1) The result is variable. Very often, however, one has been surprised because the result was so accurate, corresponding with the correction one wished. This was probably so, because the need for correction and the effect of a standardised operation would both vary directly with the degree of overaction present. But because the result has been occasionally, (1) insufficient (Dunnington, 1942; Gifford 1942), (2) excessive (White, 1942), or (3) complicated by cyclotropia (Berens, 1942), there is a tendency to follow White's lead and recede the muscle at its insertion.

Gifford wrote that to prevent reattachment near its origin it was wise to resect 4 millimetres to free the muscle completely from fascial attachments. Otherwise he found that the muscle tended to become reattached near its origin. Neely, 1947, preferred a tenectomy near the origin, and if necessary a tenotomy at the insertion later.

(2). Tenotomy at the insertion. This operation leads to variable results (White 1942) and others, or " almost invariably complete paralysis " (Dunnington, 1942).

(3). Recession, at the insertion as described by White (1942, 1944) and later by Guibor (1944), leads to " much more definite and accurate means of control." Though myomectomy near the origin is usually satisfactory for a unilateral hypertropia over 15 dioptres, in smaller unilateral errors and in bilateral cases recession is indicated. The fibrous bands between this muscle and the

external rectus require division White (1942). In addition, Guibor (1944), advised division of bands between the inferior oblique and inferior rectus unless one was performing a tenotomy in which case a paralysis would result. The wisdom of dividing them in a recession is doubtful. Berens, 1942, stated that it was not known yet how far to recede the muscle. The tendency was to under-correct the error. He receded the muscle 9-10 millimetres and as much as 7 millimetres without detaching the external rectus. He had obtained from 4-6 dioptres to total correction of 18 to 20 dioptres. He thought that a recession of 8 millimetres would correct from 5 to 8 dioptres in the primary position. He described a reduction in esotropia when present from one-third to one-half; in one bilateral case it was from 18 to 5 prism dioptres. White severed the muscle 2 millimetres from the insertion. It has been stated that undue trauma could produce choroiditis near the macula and as a paracentral scotoma. Dunnington. The posterior vortex vein, which is 5·5 millimetres behind the equator, is anterior and medial to the insertion. Care must be taken to avoid the inferior rectus muscle.

Stallard (1946) described a recession controlled by 2 mattress sutures through the ends of the divided muscle. Prangen (1947) attached the inferior oblique tendon on the horizontal meridian and 6-7 millimetres posterior to the mid-point of the insertion of the external rectus. This, he claimed, eliminated all elevation in adduction.

(4). Altered insertions of the horizontal rectus muscles. Bielschowsky, 1945, corrected a high degree of overaction by lowering the insertion of the ipsilateral internal rectus. Foster & Pemberton, 1946, found that the eye tended to move in the direction of the displacement of the insertion. Half-width raising and resection of the external rectus gave on an average 5·4 dioptres and half width raising of the internal rectus gave half this amount. They considered that marked shortening of the muscle increased the vertical effect.

If the superior oblique was paralysed Wheeler (1935) and later White (1944), sometimes preferred a tuck or advancement, and McGuire (1948) preferred a resection of the paralytic muscle to weakening of the overacting inferior oblique muscle.

### Underaction or Paralysis of the Inferior Oblique Muscle

Bielschowsky found that paralysis was extremely rare. The incidence as found by others is summarised below :—

TABLE IV

| Incidence among | Authors | Series | Sup. R. | Sup. O. | Inf. R. | Inf. O. |
|---|---|---|---|---|---|---|
| | | | Per cent. | Per cent. | Per cent. | Per cent. |
| Congen.-Vertical Motor Pareses | White & Brown, 1939 | 661 | 75 | 2 | 18 | 3 |
| | Duane, 1912 | 107 | 54 | 7 | 33 | 6 |
| All Ocular palsies | Tomizo, 1936 | 150 | 3·3 Ext. R. | 10·7 29·3 | 3·3 Oculomotor | 0·7 43·3 |
| Unilateral Vertical palsies | Anderson, 1st series 1947 | 150 | 53 | 27 | 11 | 9 |
| | 2nd series† | 62 | 45 | 26 | 11 | 5 |
| | Hughes, 1943 | 47 | 39 | 6 | 1 | 4 |
| Traumatic Ocular palsies | Cross, quoted by Neely | 138 | 24 Ext. R. 11 | 21·5 | 2 Int. R. | 6 5 |
| | Neely, 1947 | 54 | 26 Ext. R. | 31 4 | 4 | — |

† NOTE. In this series there were 8 cases with weak inferior rectus and inferior oblique muscles and the initial lesion was not known.

Paresis of the inferior oblique muscle may occur as an isolated palsy when it may be congenital or acquired, or it may be associated with other palsies.

### ASSOCIATED PALSY.

1. It may be associated with weakness of the contralateral inferior rectus. In paralysis of either muscle a secondary underaction, so called " inhibitional paresis," of the other may occur. If the R. Inf. O. be weak, the ipsilateral antagonist, R.S.O. contracts because of weakened opposition. A reduced stimulus is then required for a given action. Therefore the yoke muscle, L. Inf. R. also will receive a weak stimulus and so appear paretic (Adler, 1946). Just as difficulty in recognising the initial lesion is found in associated paresis of the opposite superior oblique and rectus muscles it also occurs, but less frequently, in disentangling weakness of the inferior oblique and of the opposite inferior rectus muscles. The same guides fortunately hold here. They are:—

(*a*) Torticollis is more likely if the oblique muscle is affected.
(*b*) Increase of vertical deviation on forced tilting of the head to the opposite side occurs if the oblique is weak.
(*c*) The smaller field of fixation usually belongs to the eye with the primarily affected muscle.

2. Inferior oblique paresis may also be associated with paresis of the homolateral inferior rectus. When we recall their intimate relationship especially in development this is not a surprising occurrence. Chavasse, 1939.

3. Paresis of the inferior oblique muscle and the homolateral superior rectus may occur together. No elevation of the affected eye will be present. According to White (1942) and Burian (1942), this association is not infrequently seen. The inferior oblique muscle is usually the more paretic.

4. Paresis of the inferior oblique may be associated with that of the medial and the inferior rectus, if the inferior division, and with the superior rectus if both divisions of the third nerve are affected.

5. Paresis of both inferior oblique muscles. This is usually accompanied by underaction of both inferior recti. In my first series this condition was found twice and four times in the second series. Hughes (1943) found paresis of both inferior oblique muscles in one of sixty-nine patients with vertical palsies.

## ISOLATED PALSY.

It is the least common isolated oculomotor paralysis (See Table IV).

1. *Congenital Causes.*

These have been summarised recently (Epstein, 1947). There may be :—

(1) Errors of cleavage. The inferior muscles do not completely separate from each other till the 20 millimetre stage.
(2) Aplasia of primitive head cavities.
(3) Aplasia of connections within the central nervous system.

2. *Traumatic Causes.*

Paralysis of the inferior oblique muscle is very rarely the result of the usual forms of trauma. Its production at operation however is possible. The inferior oblique muscle may be injured accidentally during operations for retinal detachment and Gifford's case 22 (1942), is an example of this. White (1943) warned against a similar injury during a recession of the external rectus. This is more likely to occur if this muscle has been operated on previously. It has been claimed that hypertopia following such an operation may be due to such an injury.

## TREATMENT.

The successful methods of treatment may be summarised as follows :—

1. *To Strengthen the Affected Muscle.*

(*a*) Advance at bony origin. Wheeler 1935, Kirby 1946, preferred this and reported cases. Chavasse thought this was the wisest treatment. With the courage based on accurate observations that characterised him, J. M. Wheeler led this attack on the paralysed muscle itself. He advanced the muscle over the orbital margin and using two sutures attached it to the periosteum of the maxilla. He obtained satisfactory results, 1935. He and White agreed, however, that in paralysis this alone was inadequate.

(*b*) "Advance" or tuck at insertion and if inadequate perform recession of contralateral superior rectus. (White, 1942, 1943, 1945; Dunnington, 1942). White, however, stated that neither splicing at the insertion nor tucking at the origin gave as large a correction as Wheeler's operation which could correct from 30° to 50° according to which eye was fixing.

(*c*) Resection at insertion. Berens and Loutfallah (1943) used a single mattress suture. Wagman (1945) preferred three sutures.

2. *To Weaken Contralateral Yoke Muscle.*

(*a*) Duane suggested tenotomy of the contralateral superior rectus.

(*b*) Recession of this muscle was used by Kirby (1946), Dunnington (1929), Berens, Paine and Kern (1935), Sheppard (1947), and others. Berke claimed that this operation might widen the palpebral aperture and unduly restrict elevation.

3. *To Weaken Homolateral Antagonist Muscle.*

(*a*) Tenotomy of homolateral superior oblique. Dunnington stated that it was not feasible to weaken this muscle and White thought he had never seen an indication for its tenotomy. Berke (1947), however, claimed that this was the best treatment for overaction of the superior oblique muscle.

(*b*) Recession of trochlea. Hughes (1944) and Hughes and Bogart (1942), reported 8 cases. Wagman (1945) thought that though their cases were mainly due to overactive superior oblique muscles, the initial lesion in some was probably paresis of the inferior oblique.

## Conclusion

Careful dissection, a study of function, and accurate clinical observation must precede accurate diagnosis and without accuracy in diagnosis satisfactory treatment is unlikely. The significance of slight errors in ocular movements is obscure. They do not all mean a previous lesion or even a minor rôle in producing strabismus. Their frequency in normal cases is as yet unknown.

The underaction of a contralateral antagonist may be diagnosed

as a primary lesion and the initial paresis missed or given a secondary rôle. This applies to a superior or inferior rectus and its corresponding opposite superior or inferior oblique muscle. As my observations increase my diagnosis of palsy of the superior rectus appears less frequently. Its frequency fell from 53 per cent. in my first series to 45 per cent. in my second series. One must be careful in diagnosing it (1) unless associated with ptosis or weakness of another muscle supplied by the third nerve, (2) if torticollis to one shoulder is marked and increases on tilting the head to the opposite side, or (3) the projection field of the suspected eye is smaller than that of its fellow.

One must be careful to correct large horizontal errors before tackling most vertical defects. The latter may become negligible or require only an unilateral operation. Sometimes after an operation on one overacting inferior oblique, if both had been overacting, there may be an apparent increase in the overaction of its fellow.

It may become possible to vary reattachment to correct sometimes more torsion and sometimes more elevation according to the particular need of the patient. Wheeler, 1935, in shortening the superior oblique muscle reattached it farther forwards to correct torsion, and backwards to correct elevation.

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# SOME UNUSUAL CASES OF SJÖGREN'S SYNDROME

BY

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SJÖGREN S syndrome indicates a general constitutional or systemic disturbance of unknown origin. Very complete investigations of typical cases have been made by Sjögren, Bruce, Lutman and Favata and Stenstam without finding any common aetiological factor, and all that can be said is that most cases appear in women at or after the menopause without any history of previous disturbance of the menstrual cycle.

In this regard it is well to bear in mind the extreme chronicity of the complaint and the possibility of the menopause being only an aggravating factor in a condition already established. The most striking impression gained from reading the details of published cases is the freedom of the patients from any disorder not referable to the syndrome described by Sjögren.

It is of interest, therefore, to record cases with unusual constitutional features, and numbers one and two described below are of a man and his daughter, the latter with a lifelong history of dry eyes and showing signs of pituitary dysfunction. The third and fourth are of a woman and her daughter, the latter having pulmonary tuberculosis. The fifth case is of a young woman whose symptoms seemed to originate from a fracture of the base of the skull.

*CASE* 1.—Because of a feeling of grittiness in his eyes and some hypersensitivity to light of many years duration, Mr. A., aged 68 years, had had a habit of sitting with his eyes closed when not at work. During this time he had also had slight dryness of the mouth. He made no complaint of these disabilities until a few months ago when he had a cerebral haemorrhage with hemiplegia and his eyes became worse.

He was found to have typical filamentary keratitis with a Schirmer's test of 5 mm. in 5 minutes (control, 25 mm.). The filaments and much of the discomfort disappeared in a few weeks with no more than the application of vaseline to the lid margins, though the deficient lacrimal secretion remained unchanged. The corneal sensitivity was normal. There was no history of enlargement of the parotid glands, and any rheumatism had been slight.

A diagnosis of keratitis sicca may be preferred to that of Sjögren's syndrome, and there is only his previous tendency to sit with the eyes closed to indicate that the condition preceded the cerebral haemorrhage.

*CASE* 2.—Miss G.A., aged 36 years, the daughter of Mr. A., above, said emphatically that even when crying she had never known a tear to come from either eye. Any irritation such as from foreign bodies had caused only a stinging sensation without lacrimation. Her mother stated that even as a child her daughter's eyes had been chronically sore and intolerant of light, and no tears had formed.

She came under observation 10 years ago at the age of 26 with chronic conjunctivitis, mucoid threads and myopia. A year later, in 1939, she consulted her physician, Dr. E. J. Fischmann, for amenorrhoea and a very large number of boils. She had been having severe headaches, sometimes with vomiting, and her size of shoes had changed from 5 to 7 with a proportionate enlargement of the hands. A roentgenogram of the sella turcica was thought to show some enlargement, but the fields of vision, blind spots and discs revealed no abnormality.

At this time Dr. Fischmann demonstrated the pituitary symptoms and signs to the Auckland Clinical Society. These consisted of obesity of a typical hypopituitary type, amenorrhoea, loss of hair on the scalp, growth of hair on the face, a tendency to kyphosis, striae distensae, slight exophthalmos, polydypsia, albuminuria and increased blood pressure. In addition and in contradiction to this picture of pituitary basophilism, she also had acromegaly.

Three months later, a small loss of peripheral field was detected down and out in the right field and up and out in the left. The blind spots and discs remained normal. The pituitary gland was then explored by Sir Carrick Robertson, but no tumour was found.

Shortly after the operation, the eyes became gritty and inflamed and showed fine superficial keratitis, chiefly of the upper half of each cornea, with slight pitting and fine scattered epithelial spots, many of which stained with fluorescein. Mucoid threads were present. Sensitivity was normal. About this time the mouth began to feel dry, and swelling of the parotid glands was first noticed. During the next eight months she was examined on several occasions without any material variation in the signs, though the degree of discomfort was very variable.

Service with the New Zealand Division abroad prevented further examination by the writer for some years, but, after the war, there was no doubt that she presented the typical features of Sjögren's syndrome. The corneae showed the same changes as before with, in addition, slight limbal vascularisation and some small filaments. Mucoid threads were present and Shirmer's test showed no absorption beyond the lid margin from either eye in 5 minutes (control 30 mm.). The discs were normal and the only field defect was a partial right centro-caecal scotoma. The mouth was dry and the parotid glands were considerably enlarged and tender. There was a history of rheumatism and the menstrual periods had not returned. She stated that she had seldom perspired and then only slightly.

There was no radiographic evidence of salivary calculus and the sella turcica was of normal size with intact bony outlines. The Kahn test was one plus positive and the Wassermann reaction doubtful on two occasions. At a third examination the Wassermann reaction was one plus positive. The blood count and sedimentation rate showed no abnormality.

In a personal communication, Dr. Fischmann gives the following additional information:—

"Involvement of the joints was observed on two occasions. In 1945, moderate pain and swelling of the proximal interphalangeal joint of the right middle finger appeared, accompanied by ache in the calf muscles, especially during the night. X-ray of the involved joint proved negative. In 1947, pain appeared in the knees, wrists and ankles with slight swelling of the ankles and the right thumb base joint.

The joint involvement does not conform with any of the three classical patterns of chronic joint disease (rheumatoid arthritis, osteo-arthritis and gout). It resembles the palindromic rheumatism of Mayo Clinic investigators more closely than any other joint disease known to me.

To test pituitary function, an insulin tolerance test, the basal metabolic rate and a water concentration and dilution test were done in 1945. These tests as well as an electrocardiogram were normal.

Would you think that the early cessation of ovarian function due to absence of the two gonadotrophic pituitary hormones may have played a rôle in the early onset of keratoconjunctivitis sicca?"

As the patient is intelligent and there is no reason to doubt the accuracy of the history it is probable that this is a case of Sjögren's

syndrome of congenital origin analogous to Duke-Elder's case of congenital keratoconjunctivitis sicca, and a case recorded by Hamilton. In the present state of our knowledge it is impossible to say what significance, if any, can be given to the pituitary dysfunction or the doubtful Wassermann reaction.

*CASE* 3.—Mrs. S., aged 58 years, complained of a varying degree of soreness of the eyes of about four year's duration. Various kinds of drops had been prescribed by her physician, but they had all been irritating and she had found by experience that the best remedy was frequent bathings with water. On being questioned, she stated that the mouth had been dry, the saliva frothy and the tongue at times inflamed for about eight years. The inflammation of the tongue had responded to treatment with vitamins. The parotid glands had been swollen and tender on three occasions in 1946. She had had her teeth removed about fifteen years ago and had not had any rheumatism.

On examination, the eyes showed the characteristic changes of keratoconjunctivitis sicca with a few fine filaments and a mild degree of staining with fluorescein. Shirmer's test showed only 2 mm. of moistening in each eye on two occasions.

The patient lived in a remote town and it was not possible to have any pathological investigations made.

*CASE* 4.—Miss M.S., aged 26 years, daughter of Mrs. S., case 3, was seen for the first time this year. She complained that her eyes had been chronically inflamed and sore in varying degrees for about four years. When questioned, she said that she could not remember ever having noticed any tears, that her voice had been husky for a few years and that, during this time, she had had slight dryness of the mouth in the mornings and a tender swelling of the parotid glands every month or two. This swelling had usually lasted only a few days and had twice been diagnosed as mumps. Her teeth had decayed at an early age and had all been removed when she was 17. Perspiration had always been free on the hands and feet, but not elsewhere. Her menstrual periods had been and still were quite normal.

As a child, she had been suspected of having pulmonary tuberculosis. This was confirmed in 1944 and she was admitted to a sanatorium, and, although the infection was under control, she still had a pneumothorax. Her health otherwise had been good except for slight rheumatism in the arms and legs. Her father had died of tuberculosis and her two sisters were affected. Two brothers were healthy.

She was a tall, round shouldered girl of unemotional temperament whose only obvious disabilities were her chest and her inflamed eyes. The characteristic mucoid threads of keratoconjunctivitis sicca were present, the corneae showed superficial keratitis chiefly in the upper halves and, when stained with fluorescein, showed much superficial punctate staining and many fine mucoid filaments. The vision was reduced by the keratitis to 6/9 in the right eye and 6/24 in the left. There was no intra-ocular abnormality. Shirmer's test showed an absorption of 4 mm. in the right eye and 3 mm. in the left in 5 minutes (control 30 mm.). The corneal sensation was normal.

The Wassermann reaction was negative and the blood examination revealed an increased sedimentation rate and such other changes as would be expected in a case of tuberculosis.

*CASE* 5.—Miss M.W., aged 33 years, met with an accident at the age of 21 in which the base of her skull was fractured, with consequential paralysis of the right side of the face, paralysis of the right external rectus muscle and deafness of the right ear. Except for diplopia, the vision was unaffected. When she recovered full consciousness she found that her mouth was dry, and she has been unable to eat dry foods ever since.

The facial paralysis recovered in about six weeks, but the external rectus paralysis, the deafness and the dry mouth have persisted.

A few months after the accident her teeth began to decay, her nose and throat became dry so that she had to gargle every morning, the saliva became thick, white

and scanty, and the tears did not form normally. The eyes, however, remained comfortable and free of inflammation.

About four years later the left eye became chronically inflamed and gritty and tended to close, especially in a strong light. When irritated, both eyes smarted but no tears formed. Mucous threads were sometimes present in the mornings.

Except for some slight enlargement of the thyroid gland at about the age of 17 her general health has been good, her menstrual periods have been regular and she has had no abnormalities of the skin and no rheumatism. The parotid glands have not been enlarged. Since the accident, however, her memory has been poor and she has had a persistent feeling of drowsiness.

On examination, she was found to be of healthy appearance and of unemotional temperament. The teeth showed very extensive repair. There was some chronic conjunctivitis, chiefly of the left eye, and both corneae showed fine superficial erosions staining with fluorescein. Shirmer's test revealed:—Right eye, 10 mm. of moistening, left eye, 6 mm., normal control, 30 mm. The differential blood count, sedimentation rate and Kahn test were normal.

The sella turcica was normal in shape and size and its bony outlines were well defined, regular and intact. There was no radiographic evidence of the old fracture of the skull.

## COMMENT.

Some of these cases illustrate a common and understandable vagueness about the time of onset. The progress is usually extremely slow and there is a considerable difference between the result of Shirmer's test in the normal subject and in the patient with signs and symptoms of keratoconjunctivitis sicca. A patient may show the syndrome in a fairly advanced state without being greatly inconvenienced and it is usually impossible even to infer when secretion began to fail. Sjögren has pointed out that the organic changes in the gland appear earlier than the symptoms of diminished secretion.

Case 5 may be analagous to Wagenmann's mentioned by Duke-Elder. The history of xerostomia soon after the fracture of the skull is unusually definite, but it is noteworthy that the symptoms in case 2 increased after the craniotomy for pituitary tumour.

In speculation as to the cause of the syndrome, allowance must be made for the possibility of commencement of the pathological process long before the first complaint of symptoms.

The doubtfully positive Wasserman reaction in case 2 and the tuberculosis in case 4 suggest infection as a causative factor. This is supported by the case of a man of 60 recently referred to the writer by Dr. A. N. Talbot. He had keratoconjunctivitis sicca with slight aqueous flare in both eyes and a posterior synechia. His Wassermann reaction and chest roentgenogram were negative. These, however, are isolated instances the significance of which must not be overestimated. It is more reasonable to suppose a congenital defect which may be made manifest at any period of life by some aggravating circumstance. This suggestion is supported by Lisch's series in which twelve people in three generations of one family showed some evidence of the syndrome.

Lisch states that the majority were of asthenic physique and looked ill, and Lutman and Favata mention the slender build and nervous temperaments of their cases. All those mentioned in this paper and four others under treatment at the present time are phlegmatic rather than excitable and, excepting case 2 with pituitary dysfunction, cannot be said either to be of any constitutional type or to look ill.

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## ADAPTATION TO ENVIRONMENT


BY

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LONDON


IT has been a practice, especially during the war years, to analyse the job, to analyse the men, and to attempt to fit the right man into the right job. It is thus assumed that certain people have characteristics which enable them to develop along one particular line, and that along this line they will do better than along any other. Newton has taught that action and reaction are equal and opposite in the physical sphere, and to a limited extent the same may be true in the psychological. In other words, although the man has an effect on his work, his work also has an effect on him.

The majority of us become ophthalmic surgeons in rather a haphazard fashion; in fact, the same may be true of the whole medical profession, and it is more than likely that its members represent a random sample of the upper middle classes, it being only occasionally true that anyone goes into the medical profession because he has a particular flair for it, or thinks that he has.

If this be true, it is rather extraordinary that such a large percentage of doctors make good, and that there are not a greater number of square pegs in round holes. It is true, however, that there are some and that in the course of time the sharp edges get worn by the cylindrical circumference of the containing environment. Are we all worn into more or less the same shape by 15 to 20 years of ophthalmic practice, and if so, what characteristics may one justifiably look for in an ophthalmic surgeon of some years' experience?

To take first things first, let us consider the environment in which the ophthalmic surgeon finds himself. The estimation and correction of errors of refraction form a large part of his work, and considered as " work " it cannot escape the indictment of " monotony." Monotony in work, however, is what a large proportion of humanity perhaps unconsciously desires, since to do one thing really well is a source of deep satisfaction. The writer well remembers a conversation with one of the first Labour Members of Parliament, in which he asked whether monotonous work was not one of the bugbears of those who labour in factories. He received the unexpected reply, " by no means, the work can be done mechanically and without conscious effort so that it sets the mind free to think about what it likes." In the case of the Labour member the sonnets of Shakespeare were instanced as one of the things over which his mind liked to roam, and in the case of the eminent oculist whom this issue of the Journal commemorates, it is perhaps permissible to suppose that though the sonnets of Shakespeare were at times in his mind, other questions such as intricate problems in optics, pathology, colour vision and psychology entered and were perhaps resolved. The elderly Labour member supported his contention by instancing the owner of a factory who felt compassion for his workers on account of the monotony of their tasks, and by the exercise of considerable ingenuity arranged matters so that each man would have a change of work every week. What happened was that after a fortnight he was faced with the prospect of a strike if he did not return to the old method!

Monotony may thus have its merits, and although a large part of our consulting work may be almost mechanical, we contrive to make it interesting by seeing to how high a pitch of accuracy we can raise our efforts to correct what is in reality a mistake on the part of Dame Nature, that stern old autocrat whom we alternately woo, in hoping she will provide healing after a cataract operation, and defy in removing a lens she has allowed to become prematurely opaque.

There is another aspect of refraction work, however, which cannot fail to have an effect on those who practise it, and this is that

our patients are being constantly placed in a dilemma, and whether they like it or not, must give a definite answer " better, or worse or the same." It has been related that Frenchmen say " two and two make four," whereas the Englishman prefers to state that " no one can contradict me if I say that two and two do not make five." These two attitudes of mind are continually found in our patients, and it must be instructive to the oculist to compare the answers to the same series of questions by, say, a fresh, uninhibited child of five or six with those of an aged diplomat or a prominent industrialist. Here again we may surmise that the critical faculty and insight into character which are such prominent features of him whom we commemorate in this issue, may have been fanned into activity by these experiences.

Another aspect of refraction work is the opportunity it gives of observing at close quarters the features, facial expression and general demeanour of a large variety of different types of human beings. The patient is so engrossed in looking at the letters that he or she is unconscious of anything else, and can be observed in a state of complete detachment. Most of the observations are trivial, as, for example, that very few people fail to possess enlarged pores in the skin of their nose, though they are often filled with face powder, and look all the worse for it; but now and again the twitchings of the lids, the restless movements of the hands, and so on will give a clue to the underlying neurotic cause of the headaches. It is not given to many members, even of the medical profession, to have the opportunity of fifteen minutes or so undisturbed observation of preoccupied individuals at close quarters, and several years of this engrossing occupation must have an effect on the mental outlook of the observer.

Alertness of another type is also called for if more important defects are not to be missed. To give but one example, the failure of a patient to read the last few letters of a line of test type with the right eye, and the first few with the left eye may indicate a bitemporal hemianopic scotoma, which calls for further investigation. The same alertness, or an even higher degree of it is called for in ophthalmoscopic examinations.

In fact, the oculist must often feel that his professional life is, so to speak, a constant one man " Brains Trust " with Dame Nature as the question mistress, waiting to catch him out if he fails to notice what may at first sight appear to be unimportant signs and symptoms.

Emphasis should perhaps be laid on the one man aspect of this struggle, since the oculist is a Caesar, in the sense that there is no appeal to a higher authority except in the rare instances when a second opinion can justifiably be sought. He is thus taught to

accept and eventually to welcome responsibility and the tendency to " pass the buck " which is probably inherent in most human beings is, we hope, suppressed. Carried too far, this acceptance of responsibility may develop into tyrannical authoritarianism, but such a state is happily rare, its occurrence being prevented by the failures and disasters which inevitably happen to all of us.

When it comes to operating, some new factors have to be considered. It occurred recently to the writer to wonder why patients behaved so much better now than they did twenty years ago. Various answers suggested themselves, such as pre-medication with sedatives, facial nerve block and so on, but it was not until some time had elapsed that he hit on the true answer, which was, that it was not the patients who were behaving better, but he himself. The ability to impart such a degree of confidence in another human being that he or she will permit of the performance of an operation on the eye, even though it be analgesic, is a wonderful possession and is not lightly gained. It demands on the part of the operator not only mental and physical fitness, but a degree of confidence in his ability to do what he sets out to achieve, and the possibility of communicating this confidence to his patient lying supine on the table before him. The same communication of confidence is important during convalescence. An extreme example of this occurred to the writer when he had to perform a cataract extraction upon a devout Roman Catholic priest, who was so convinced that divine aid would be forthcoming that he knew he had no cause for anxiety. In consequence of this, he lay in bed tranquil and relaxed after the operation, to such good effect that it was difficult to say after a week which was the aphakic eye, and the second eye was then dealt with, with a similar result.

Some more points remain in considering the environment of the ophthalmic surgeon. The first is the high percentage of success he achieves in the treatment of his patients. This tends to make him a therapeutic optimist as opposed to the nihilism which affects some of his medical colleagues and possibly to be over credulous as to the value of certain forms of treatment. He may mistake for organic cure a result which is in reality due to suggestion, but the main thing to him is that the patient is better, whatever the means by which this has been achieved. An example which occurs to one's mind is the cure of chronic dyspepsia by the correction of small degrees of astigmatism. Another point is that most of the operations he performs have results which are sudden and dramatic and may completely change the further outlook and potentialities of the patient; small wonder then that the oculist should receive many expressions of gratitude and kindness from his patients and that if at times he should lose faith in humanity these will help to restore it.

A third point which may have some effect on character is that the major part of eye work is meticulous and of an almost mathematical exactness which predisposes to clear thinking.

There are many other features of ophthalmic work which have been omitted in this short review, for example, the rush and hurry of a crowded out-patient department, the attempt to do good work with inadequate equipment, the realisation when teaching undergraduate students that ophthalmology is only a small branch of medicine and that all they want is the irreducible minimum of information. The first two may induce a feeling of frustration, but the last may beget some humility and a realisation that great though the field of ophthalmology may be, it is only part of the vast acreage of medicine, much of which we have not explored.

Such then is the environment in which we live and it seems to produce a kindly race of men with a wide knowledge of humanity, an ability to come to quick and wise decisions and a flair for accurate observation. That these and other qualities must have been present in some degree before engaging on ophthalmology is, of course, obvious, but that the practice of our profession encourages their growth seems a likely possibility.

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## ANGIOMATOSIS RETINAE, WITH REPORT OF PATHOLOGICAL EXAMINATION

BY

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IN view of (1) the rarity of the condition (2) the lack of reports of late results of treatment, and (3) the fact that the affected eye of the second case was excised and examined pathologically, the following two cases seem worthy of record. One, Ada C., was first examined in 1936, had both eyes affected and had varied treatment; the second, Violet H., was seen at Moorfields by several surgeons and a fundus drawing was made in 1939; the writer did not see her until November, 1946, when the affected eye was found to be painful, blind and glaucomatous, and was therefore excised.

Case 1. Ada C., aged 28 years, attended Moorfields Eye Hospital on February 8, 1936, complaining of blurring of the sight of the left eye, apparently of sudden onset. At that date the R.V. was 6/6 6/5 (partly), the L.V. 6/60. After dilatation of the pupils, examination of the right fundus through clear media showed a disc of healthy appearance, two very dilated vessels passing into the

inferior temporal region, and some hard white exudate like that of circinate retinopathy mostly between the vessels (see Fig. 1). In the 7 o'clock direction a rounded prominence of pinkish colour was visible in which the two large vessels were lost. The left eye, whose

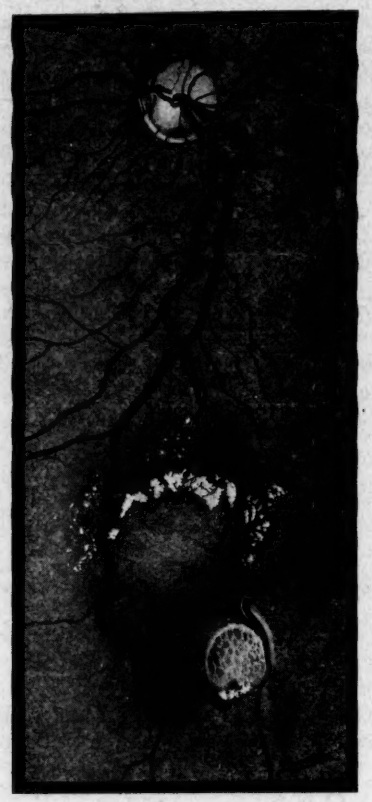

FIG. 1.

Ada C. Fundus drawing of the right eye, showing two dilated retinal vessels ending in a pinkish-coloured localised prominence. (The drawing has been rotated to save space. The angioma was in the 7 to 7.30 o'clock meridian).

media were also clear, showed two vessels of very large calibre passing from the optic disc in an upward direction, the larger being also very tortuous (see Fig. 2). A large area of hard white exudate occupied most of the area from the optic disc to the macula. Small retinal vessels lay anterior to the exudate. The enlarged

FIG. 2.

Ada C. Fundus drawing of the left eye, showing a similar appearance to that of fig. 1, but with two swellings in the upper periphery.

blood vessels led up to an oval pinkish prominence, in the 12 o'clock direction, fully 2 disc diameters in vertical dimension and rather less transversely. About 1 disc diameter further and slightly to the temporal side lay another similar prominence of smaller size. The retina in the region of the swellings and of the enlarged vessels had the appearance of being slightly detached.

By estimating disc diameters both from the disc to the swellings and from the swellings to the extreme periphery and assuming the

distance from disc margin to the limbus to be about 36·5 mm. in the two directions, it was calculated that the angioma in the right eye was 18·5 mm. from the limbus; in the left it was judged that the anterior limit of the smaller angioma was 23 mm. from the limbus.

*Treatment of the left eye.* Between February and June, 1936, the left eye was treated by electrolysis with a fine perforating needle 3 times. A galvanic current by the cathode was used at 2 milliamperes for 4 seconds to 4 milliamperes for 6 seconds, 10 to 12 punctures at each operation. A further application of electrolysis, 5 milliamperes for 10 seconds at each of 27 perforations, was made in June, 1937. Only at the second application of the 3 mm. fine needle did well-marked bubbles appear in the vitreous. At the end of this operation the whole of the angioma area was surrounded by the pale reaction of electrolysis. The 2 large retinal vessels were much reduced in calibre and little larger than normal retinal vessels.

As during succeeding months of 1937 the 2 angiomata in the left eye showed no signs of regression, treatment by the 1 gram radium bomb was applied. It is regretted that details of dosage cannot be traced. The patient, however, declares (1948) that 8 separate hours of treatment were given and further treatment stopped as loss of eyelashes took place in the lower eyelid. A total dosage of 14 hours had been planned. In the latter part of 1938 no definite improvement in the condition was detected. It was therefore decided to employ diathermy with a perforating needle.

On December 7, 1938, perforating diathermy was employed with 7 punctures. One of these coincided with the larger retinal vessel and one with the angioma. At the end of the operation the vitreous was very dark and vision barely perception of hand movements.

On January 2, 1939, the L.E. had vision still no more than perception of hand movements. The vitreous was very dark with a faint red reflex above.

*Treatment of the Right Eye.* On September 12, 1936, the right eye was treated by electrolysis under local anaesthesia aided by luminal and omnopon. A guide suture inserted at the limbus was carried across the cornea in the 6.30 meridian. A small puncture was made 22 mm. from the limbus in this line with a broad needle and a Foster Moore stud inserted. This showed ophthalmoscopically a white streak immediately posterior to the angioma and slightly temporal.

A galvanic current was then applied by means of a 3 mm. sharp needle on an insulated curved shaft, connected with the cathode. A current of 10 milliamperes was used at 12 points for 6 seconds

each. The punctures were made as far as possible in a square area, at 1 to 1·5 mm. apart just anterior to the stud mark. At the end of the operation a mass of small bubbles was seen with the ophthalmoscope just posterior to the angioma and a wide area of pallor anterior to these. Finally 2 or 3 more punctures were made posterior to the stud in the hope of destroying the enlarged vessels.

On October 5, 1936, the vitreous was hazy but a large area of reaction was visible below with an outlying patch just below the macular area (from one of the latest applications).

On November 11, 1936, the R.V. with +2·25 sph.=6/12 the pupil being dilated. L.V. with +1·25=6/24. The angioma was visible in the right eye in an area of atrophy, but was estimated to be 2/3 disc diameter as compared with the estimate on September 10, 1936, of 1 d.d. across.

*Progress.* On May 18, 1939, two weeks after a blow on the forehead the patient noticed a cloud in front of the right eye. Several streaks of haemorrhage were visible on this date in the right vitreous. Dark streaks were still visible in the lower part of the vitreous cavity in March, 1940. The appearance of slight retinal detachment is noted below. Posterior cortical lens opacities are seen in the left eye, and a large retinal cyst in the lower periphery.

September 10, 1940. R.V. with lens=6/9, L.V. with lens less than 6/60. In the right, white proliferating tissue extends upwards from the most posterior point of electrolysis towards the fovea. Increasing retinal detachment below: L.E. anterior and posterior iridescent cortical lens opacities.

January 2, 1941. R.E. a delicate veil from the disc passes towards the macula. The lower retina is quite definitely detached. L. disc is barely visible owing to lens opacities.

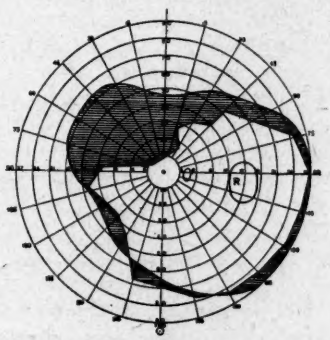

FIG. 3.

Ada C. Field of vision of right eye on October 22, 1941. $\frac{1}{2}$° white object.

*Field of Vision*. Fields mapped by the perimeter before operation with 1/4° white object were full. The chart of October 22, 1941, with 1/2° white shows a representative right field of several charted after operation (Fig. 3). Bjerrum screen indicated encroachment towards the macula in the upper nasal region to the 8° circle (4/2000 white object) on November 11, 1936.

On July 8, 1942, the loss had extended to the 3° circle (6/2000 white), and on January 20, 1948, to the fixation point (5/2000 white).

*Visual acuity*. November 11, 1936. R.V. (pupil dilated) with +2·25 sph.=6/12, L.V. +1·25=6/24.

In 1943 on several occasions R.V. recorded as 6/9 with glass. In December, 1944, R.V. with glass=6/18, and complaint made of recent dimness of sight. This was explained by vitreous floating opacities of a reddish colour.

November 6, 1946. R.V. with glass 6/12, 6/9 (4).

January 20, 1948. (H.N.) R.V. $\frac{+2{\cdot}5}{+0{\cdot}25 \text{ ax. } 90°}$ =6/24 6/18 (3).

L.V. perception of light with faulty projection.

## DISCUSSION

In view (1) of the tendency to bleed into the vitreous, as also observed by Foster Moore[1] after radon treatment, (2) of the very slow absorption of blood, and (3) the rucking of the retina which is evident between the disc and the lower part of the right macula and hence a fear of proliferating retinopathy, no further operative treatment to the right eye has been thought advisable.

In view of the slowly progressive loss of field with increasing retinal detachment below, it is intended to recommend diathermy puncture in 2 places in the hope that retinal cyst formation is the cause of detachment as occurred in the left eye.

Case 2. Violet H., married, aged 20 years. The patient attended Moorfields Eye Hospital early in October, 1946, complaining that the left eye had been aching on and off for two months.

*Previous History*. She had been to the London Hospital in 1935 where it was stated that she had a " birth-mark " at the back of the left eye.

In October, 1939, she first visited Moorfields. The writer first saw her in 1946. The recent in-patient notes record that she had been examined in 1939 by several members of the Honorary Staff and that the diagnosis of angiomatosis retinae was made. (See Fig. 4, drawing of October 5, 1939.) She was admitted on November 5, 1946. The right eye was free from congestion, the

FIG. 4.

Violet H. Fundus drawing, left eye, October 5, 1939.

pupil circular and active, the media were clear and the fundus healthy. With −4·5 dioptre sph. −0·5 dioptre cyl., 180°, vision was 6/6. Tension normal. The left eye was white, the cornea clear, and the pupil circular with no direct reaction to light and sluggish consensual reaction. No red reflex was obtained. A glistening mass was seen close behind the lens with numerous straight vessels coursing over it. The tension was much raised and there was no perception of light. To transillumination there was relative dullness below. The left eye was excised on November 6, 1946.

*Pathological examination.* The eye, fixed in Zenker's fluid, was embedded in celloidin and antero-posterior sections were cut. These were stained with haematoxylin and eosin.

HISTOLOGICAL EXAMINATION. *Path. No. R.L.O.H.* 271/1946.

Antero-posterior sections examined under Zeiss A. objective and No. 4 eye-piece showed a shallow anterior chamber whose angle was closed by apposition of the iris root to the cornea, completely

covering the region of the canal of Schlemm. There was atrophy of the iris and ciliary body with slight ectropion of the uvea. The lens was *in situ* and had retina closely in apposition to its posterior surface. The vitreous cavity was almost entirely obliterated by complete retinal detachment. A few small round cells and fibroblasts

FIG. 5.

Violet H. Microphotograph; magnification ×35; shows the most posterior part of the angiomatosis area of the detached retina. (Stained with haematoxylin and eosin). (*a*) indicates the largest blood-vessel in the group. Abundance of coarse vessels extend forwards in the cone-shaped mass of detached retina to an additional extent about equal to that shown in this photograph. (*b*) marks areas of haemorrhage in the retina.

were near the reflexion of the retina at the ora serrata. In the posterior folded up part of the detached retina were blood-vessels of large calibre with a number of smaller vessels lying among retinal elements whose layers cannot here be indentified. Partly surrounding several of the large vessels were masses of red corpuscles —haemorrhages, which may have been responsible for the recent subacute glaucoma (Fig. 5, microphoto 1). There was no trace of

any wall or boundary to indicate any localisation of the vascular growth. In fact an abundance of vessels extended in the section for about twice the expanse shown in Fig. 5, *i.e.*, some 6 millimetres in all. The subretinal space was partly occupied by some granular exudate containing numerous migrated rounded pigment cells with circular nuclei. The choroid vessels were full of red blood corpuscles and a fairly widespread round-celled infiltration affected the spaces between the vessels.

Examination under higher magnification showed the large blood-vessels to be very thin-walled, having little more than a single layer of endothelium. The layers of the retinal structure could only be identified in the periphery, near the ora serrata. (Fig. 6, 7, 8.) No cystic changes were present in the sections examined.

The striking feature of this angioma is its diffuseness and complete absence of any definite boundary. Its extent in the sections shows that it had enlarged somewhat in the 7 years since the drawing was made. There is, however, no suggestion in the sections of malignancy. A comparison with the reproductions of the microphotographs of McDonald and Lippincott[2] shows a very close resemblance in structure. These writers, using glial stains, found only slight proliferation of the glial cells and concluded that this was secondary.

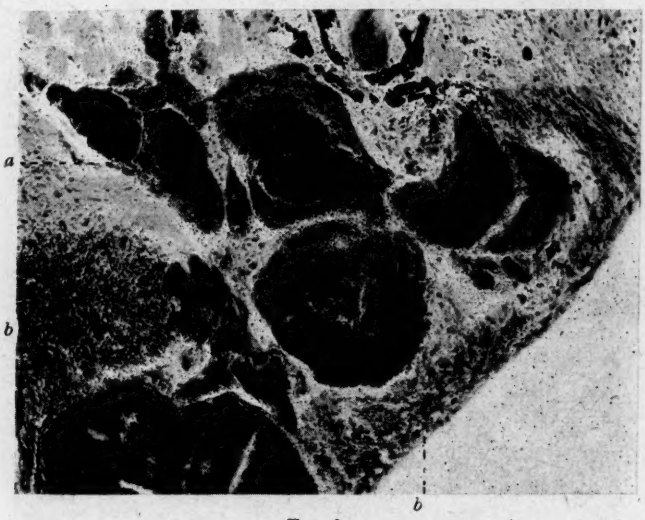


FIG. 6.

Violet H. . Microphotograph; magnification ×80. Portion of the section shown in Fig. 5. For (*a*) see Fig. 7; (*b*) haemorrhage.

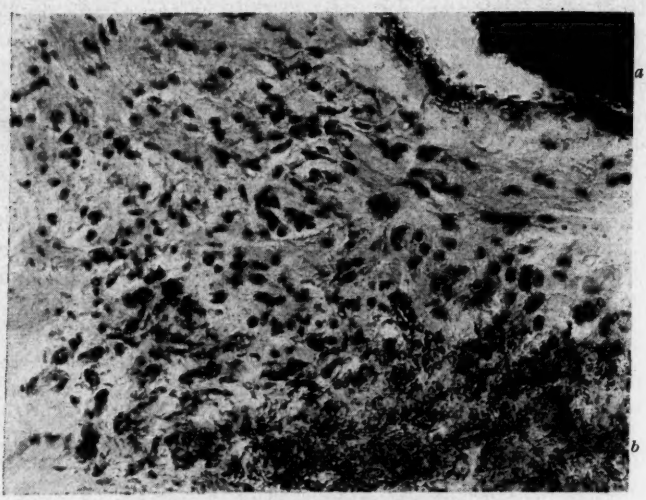


FIG. 7.

Violet H. Microphotograph; ×260. The portion shown corresponds with (*a*) in Fig. 6; (*b*) marks the edge of a haemorrhagic area in the detached retina. The blood has shrunk away from the vessel wall which shows a single layer of endothelium.

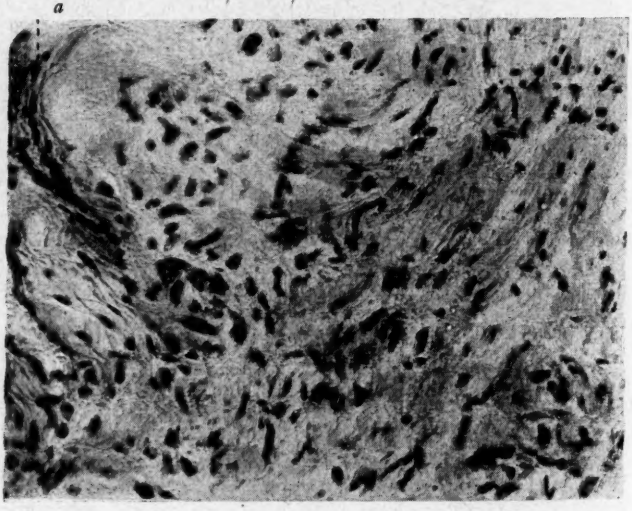


FIG. 8.

*Violet H.* ×260. Showing cellular structure. (*a*) indicates a flattened blood-vessel which can be recognised opposite (*c*) in Fig. 5. (This vessel is at right-angles to its direction in Fig. 5. The lower border of Fig. 8 corresponds with the left-hand border of Fig. 5).

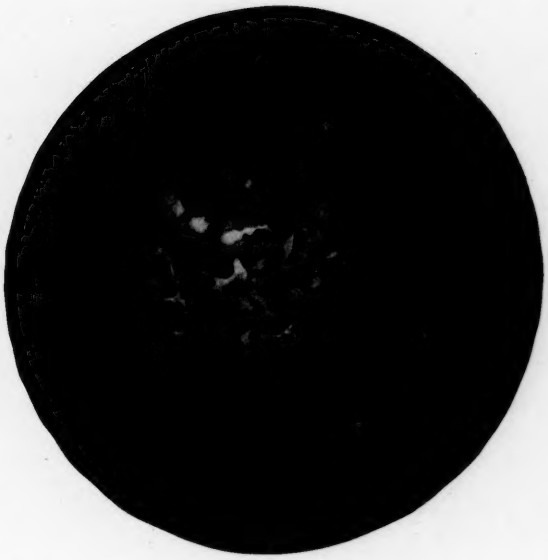

FIG. 9.

Nicolotte D. M. H. Whiting's case of bluish juxta-papillary angioma. October, 1945.

In addition to the above the writer has had the opportunity of examining two cases of a bluish-coloured angioma of venous appearance in addition to one reported by Nicoll and Moore[3]. The latter is also reproduced by Elwyn[4]. The two cases were seen at Moorfields Eye Hospital in the clinics of Mr. M. H. Whiting and Mr. E. F. King to whom the writer is indebted for permission to refer to them. They were of exactly the same type as Nicoll and Moore's seen in 1934. In all three the bluish coloured prominence with a nodular surface was at, or overhanging the optic disc.

Case 3. Nicolette D. (Fig. 9). Aged 7 years. The patient was under Mr. Whiting at Moorfields Eye Hospital Out-Patient Department on September 26, 1945. R.V. 6/9. L.V. 6/6. A mulberry-like growth was seen to overhang the disc margin of the left eye. This had been noted by Mr. Joshua Keyms of Southampton who referred the case to Moorfields. The purplish-coloured mass was approximately circular and extended about half way over the disc. It was nodular, and definitely prominent. It appeared to be composed mainly of rather large veins (larger than the ordinary tributaries of the central vein).

A follow-up has recently been possible, thanks to the help of Mr. W. E. Heath of Rochester, in the first of two cases of capillary angioma treated by Moore[1] in 1934. The patient stated that her sight remained good for nearly 18 months after the radon treatment and then failed fairly rapidly owing to cataract.

TYPES OF ANGIOMATOSIS RETINAE. There seem to be two distinct clinical types; (1) the pale pinkish swelling or swellings connected with retinal vessels of fully 2 to 3 times the ordinary calibre. These are usually circumscribed and appear clinically to have an enclosing sheath or capsule. Rarely they appear to be without any capsule—see drawing of case 2 (Violet H., Fig. 4), as is confirmed in the histological sections. In these the prognosis is bad without treatment; (2) the bluish coloured venous-looking swelling of which three cases have been seen. One of these (Nicoll and Moore[3]) was excised and found to be non-malignant. These cases should be followed up to see if the swellings increase in size. Elwyn associates cases of other types of vascular anomaly with these; (1) Coats' disease with telangiectases, (2) Sturge-Weber disease, occasionally with dilated and tortuous retinal vessels, and (3) the extremely rare arterio-venous aneurysm of the retina.

TREATMENT. The pinkish capillary angioma associated with 2 vessels of large calibre, must be treated, as it leads inevitably to blindness. Radium, radon and X-rays have been used. In all of these cataract is to be expected as in Moore's case (radon[1]) sent by Heath, and the left eye of the author's case No. 1. In the

latter, to the left eye with two angiomata—one as much as 3 mm. across, with localised detachment already present—electrolysis applied on three separate occasions between February and June, 1936, did not suffice. Radium bomb was then employed in 1937. However, no notable change in the condition followed. Perforating diathermy was employed in December, 1938, as described, with vitreous haemorrhage. Cystic degeneration of the retina and cortical cataract were present 2 years later. The angioma in the right eye appeared to be swallowed up in fibrous tissue after electrolysis, but 2 bouts of vitreous haemorrhage have occurred since and a lowly progressive detachment of the retina. Foster Moore's second case treated by radon was not traceable. Of two cases treated by diathermy Weve's[5] had vision 1/6 2½ years after treatment of an angioma in the superior-temporal region above the macula, and retained practically a normal field. Michaelson's[6] case with an angioma not far to the temporal side of the macula and with a localised retinal detachment and a retinal hole, recovered to the extent of vision 6/9 with correction as compared with 6/36 before operation. This, however, was only 3½ months after operation and the angioma was only 1/3 disc diameter across.

The author favoured the use of the galvanic current as this has been a favourite method of treating spider-naevi in the skin of the face. It was hoped to puncture the angioma and apply sufficient current by the cathode to cause haemostasis. It is probable that with any but the smallest angiomata—*e.g.*, Michaelson's —this is still the ideal method. But the method of approach may perhaps be improved. It may be mentioned that the electrocautery is used by some dermatologists to destroy a spider naevus. As in the eye, however, only one shot can be made by this instrument and a bull's-eye must be scored, this technique is not feasible for the retina. It seems that, provided the angioma is not far in the periphery, a fine but rigid needle insulated nearly to its point might be used by the trans-scleral route while the fundus is under observation with the binocular ophthalmoscope through Goldmann's contact lens[7]. The latter used this method to apply diathermy to a macular hole in order to prevent detachment of the retina, as described by Foster[8]. In the second type of angioma, that composed of coarser bluish vessels, of which three cases have been mentioned, should definite evidence of increase in size be obtained, this may prove to be the best method of attack. The help of a physicist is needed in order to choose between the merits of galvanism or diathermy. In the 3 cases mentioned it would probably be desirable to use the kind of current whose destructive effect is the less extensive, so as to cause as little damage

to the optic nerve as possible. In any case there is a great probability that almost half the visual field would be lost. When the angioma is to the temporal side of the optic disc—macular vision would be destroyed. Better that, however, than loss of the eye.

Several unsolved problems exist in connexion with this condition :—

(1) Is there a tendency for new angiomata to form as occurred in one case mentioned and illustrated by Elwyn[4] ?

(2) Hard white exudates may be present early as in the right eye of case 1 described, long before any detachment was suspected. Are these due to haemorrhage in one whose retinal vessels are especially prone to leak ?

(3) Why does retinal detachment occur when there is apparently little subretinal exudate and no hole in the retina ?

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## VISUAL PROTECTION IN AERIAL WARFARE

BY

Air-Marshal P. C. LIVINGSTON

### INTRODUCTION.

IN order that men may bear weapons with success and fortitude in modern warfare, it is necessary that they be armed, not only with equipment suitable to the occasion, but with their minds prepared for such high adventure that the capacity for imagination is locked within the lower levels of consciousness. Throughout the World War, 1939/45, personal experience records no case where a member of aircrew became obsessed by a dread of blindness through enemy action. On the contrary, the destruction of sight appeared so little feared, that difficulty was experienced in persuading personnel of the air arm to take reasonable precautions against ocular injury. This negation of the thought of blindness

no doubt results from the acceptance of sight as a natural attribute, so much part of human structure that the catastrophe of its loss is beyond contemplation. Therefore, in the heat of action, it seems unthinkable that vision should be destroyed, leaving defenceless the combatant so afflicted. The very position of Man in the Universe signifies that the guiding hand which has led him safely through many hazards to his eventual goal, is dominated by a broadening mind reacting to impressions transmitted through the visual apparatus.

## General Consideration.

In times of conflict it becomes necessary to introduce equipment aimed at the preservation of sight, without however creating a state of eye consciousness among those for whom the protective measures are intended. In lectures and demonstrations directed to this end, the audience should be regarded as containing a group of personnel who previously have given little thought to the risks to vision associated with aerial warfare, but are in fact strongly susceptible to suggestion. It becomes necessary therefore to exercise care in preserving the morale of aircrew personnel. Other difficulties occur peculiar to this branch of preventive medicine. No order exists which demands that aircrew personnel shall, under threat of penalty, adopt some special precaution designed for their safety. They may be called upon to carry a device with them on operational duty, but there is no guarantee as to its use. The problem becomes one of appeal to reason backed by sound argument. In this, as in so many other matters, the example set by Captains of aircraft becomes of particular significance. Aircrew are often hero worshippers. Frequently without a thought, they accept as indisputable the opinion of one well reputed for skill in combat. At times a situation so created may not be directed to the best interests of the Service, because some pilots of high achievement are individualists whose ideas do not conform to the recognised tactics of combat. It should fall to the lot of those whose duty it is to reduce wound incidence to offer their knowledge and experience in a manner which will create a proper understanding of the situation and of the elementary principles concerned. It is well appreciated that great individualists in War are not always the most suitable guides for a population so varied in background and psychological structure as that prevailing in aircrew. These features are stressed because they reveal a number of difficulties that may impede the use of apparatus constituting part of a campaign directed against traumatic blinding.

## EVENTS WHICH THREATEN BLINDNESS

Some operations of aerial warfare contain hazards common to combatant forces in general, others are peculiar to actions developing at altitude. Examples of the former are found in low level attack on enemy transport columns, railway systems or airfields. Here the defensive fire is commonly from machine guns, rifles and other light weapons.

High level operational flying draws fire from defensive weapons on the ground, such as light or heavy anti-aircraft guns and rockets, while in addition attack by machine gun or cannon fire may come from intercepting aircraft. Ocular injuries are found to occur from missiles intact, from fragments of these after explosion outside or inside the aircraft, or from shattered parts of the aircraft. Injuries of serious character are sustained through burns from fires started in fuel tanks or by the ignition of incendiary bombs carried within the aircraft. Fires following a crash on landing at base sometimes occur. A forced landing as a result of engine failure accounts for other forms of injury, as when the head strikes against projecting parts of the instrument panel, especially if the harness designed to restrain forward propulsion of the body happens to break.

Sudden structural failure of the air frame, in high speed manoeuvres, when for example portions of the engine cowling break away or a wing fractures, may terminate in severe facial injury involving the eyes. More rarely, wild fowl have been known to smash through the cabin structure and destroy vision.

The foreign bodies responsible for ocular injury sustained on flying duty may be metallic or non metallic. The metallic foreign bodies are more frequently non magnetic than magnetic. Therefore, the magnet in the extraction of these particles is of limited value. Experience tends to show that the eye is more tolerant of the presence of fragments of metallic alloys than was at first believed. An exception is copper.

Perspex, one of the cellulose acetate group of materials used in aircraft cabin windows, is fortunately very well tolerated. It sometimes occurs that twenty or more tiny pieces of perspex become embedded in the cornea and remain without serious reaction occurring. The only unpleasant sequel is the abnormal dispersion when light strikes the surfaces of these translucent foreign bodies set at varied angles in the substance of the cornea.

## METHODS OF COMBATING OCULAR INJURY

These group themselves under three headings:

(1) *Measures incorporated within the structure of the aircraft.*

(*a*) Bullet proof glass is constructed in layers united under pressure and held together by an adhesive substance. The glass plates so prepared attain a thickness of $1\frac{1}{2}$" or more. Welded steel or light alloy tubing comprise the supporting framework. Illustrations 1 and 2 show the effect produced upon the front screen of a fighter aircraft by the impact of a bullet at close range. Only a very few flakes have been detached on the side of the screen

ILLUSTRATION 1.

Front surface of bullet proof glass windscreen, fighter aircraft showing effects produced by 0·303 armour piercing bullet at 200 yards.

ILLUSTRATION 2.

The same windscreen as (1), showing surface towards pilot. Note how few particles of glass have been shed from the mass of cracks.

next to the pilot. (2) This effect was produced by a ·303 W. Mark 1 armour piercing bullet with a charge giving an equivalent range of 200 yards. A further example of the resistance of bullet proof glass is illustrated (3) in the case of a bomber aircraft. This sheet was situated behind the pilot on the starboard side. The photograph is taken looking aft. The attack was made by a Messerschmitt 210 whilst the Lancaster was on a mission to Frankfurt. The aircraft received 80 hits. Of these, two 792 mm. armour piercing bullets from dead astern and level, entered the rear end of the cockpit canopy on the starboard side shattering the 3" bullet proof slab. In this instance a cavity of approximately $\frac{3}{8}$" deep was made in the steel defence armour, positioned behind the pilot. A further illustration (4) provides an example of the devastating effect of close range night fighter fire upon the rear turret of a bomber aircraft. Protection in respect of the

gunner's turret is of necessity less complete than in the case of the pilot's cockpit, owing to the need to provide an observation post which permits a good area of search. There are a number of metal supports which offer secondary protection, but the fact that the turret is designed to rotate, exposes the gunner in a more vulnerable manner than is the case with other occupants of the aircraft. Furthermore, in order to obtain the best conditions of

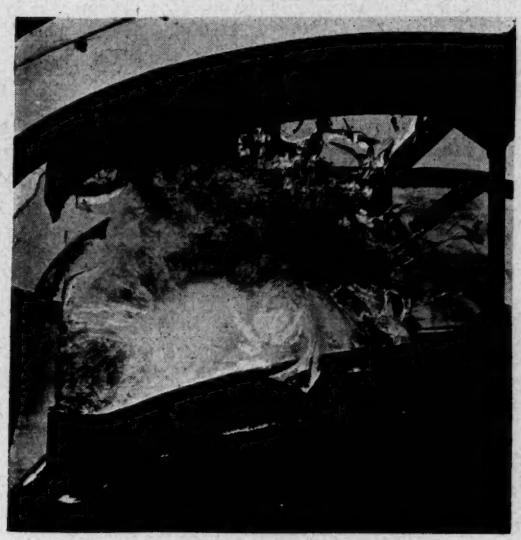


ILLUSTRATION 3.

Bullet proof glass screen situated behind pilot of Lancaster III aircraft. Effect produced by 792 mm. armour piercing bullets.

visibility it became necessary to remove part of one of the perspex panels so as to provide an area through which search of the night sky could be made with full freedom.

(*b*) The use of armour is restricted by its weight. It affords excellent protection for the pilot. These plates are usually 12 mm. thick. They can resist a 20 mm. shell unless struck point on. Their value in visual protection is indirect. For example, they stop the flight of an explosive cannon shell, which unimpeded might come at a narrow angle from behind the pilot and exploding against the instrument panel, scatter at high velocity many particles of varied composition likely to endanger the eyes.

(2) *Equipment in the form of goggles, spectacles, visors and contact lenses worn by aircrew.* (*a*) All safety glass used in goggles is of the laminated form, that is, two sheets of glass connected by a flexible interlayer. It will be observed, in illustration (5) d to g, that goggle windows are composed of two surfaces meeting at an obtuse angle. This design was adopted in order to achieve great strength. It has been shown that curved safety

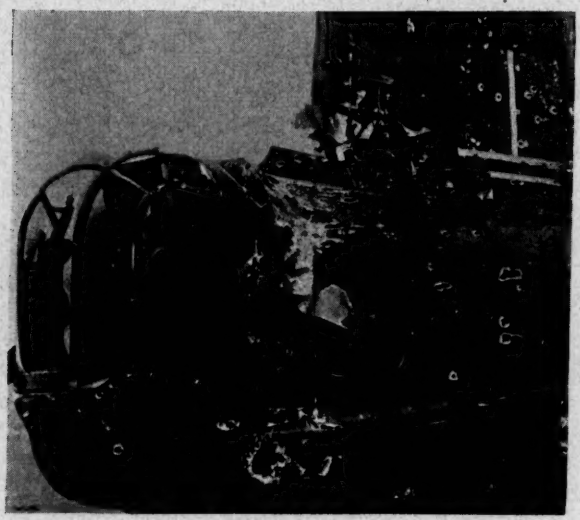


ILLUSTRATION 4.

Rear turret of Stirling aircraft after raid on Duisberg, April, 1943, showing severe damage to the rear gun turret and controls. This aircraft succeeded in reaching base.

glass as used in some types of goggle is not fully reliable. The principle of resistance to fracture is founded upon a precise union between surfaces. This union at the present time, can only be assured if the surfaces are flat. The specification under which goggle glass is passed as suitable is exacting, because the optical properties must be considered, as well as the safety factor. The test for splintering is made after accelerated ageing tests in which the glass is subjected to low temperature, hot moist air and ultra-violet light. For the splintering test, designed to eliminate glass which on fracture has a tendency to fly, the sample is held vertically and is struck centrally on one of its faces with

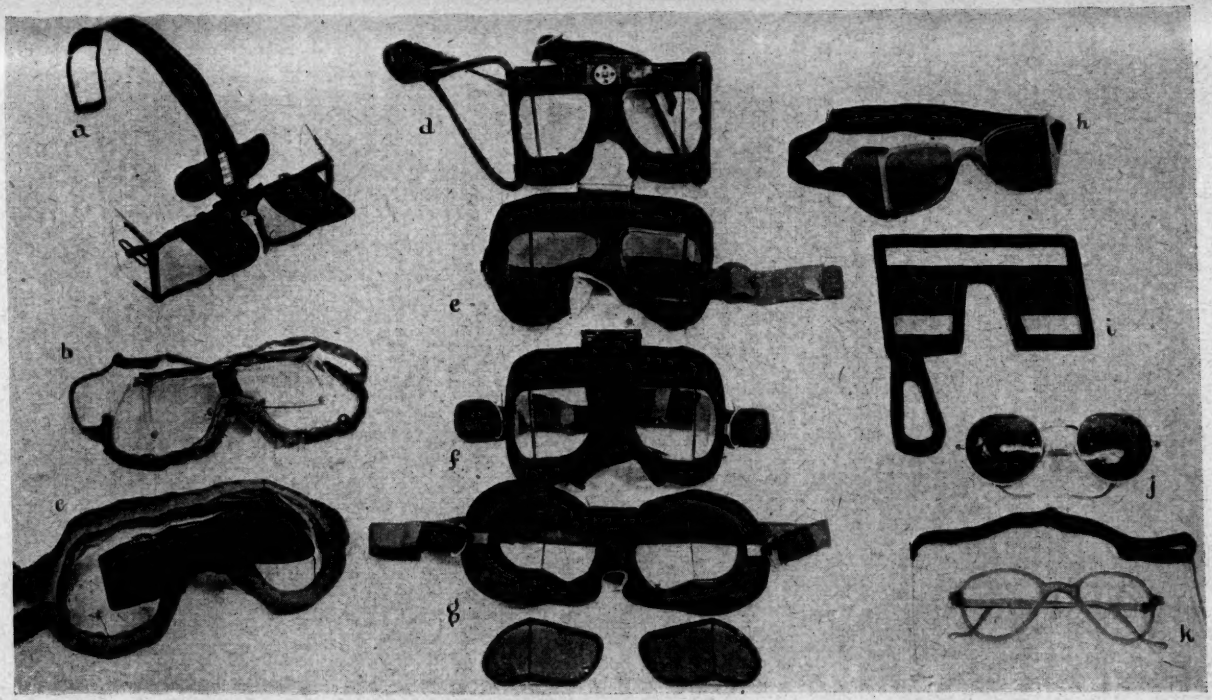



ILLUSTRATION 5.

Showing various designs of goggles, spectacles and visors resulting from the programme of development. The standard flying goggle is shown at g, with interchangeable windows untinted or tinted. The standard flying spectacle designed to receive corrected lenses at k, the present anti-glare glass spectacles at j.

a steel ball. Fragments which may be split from the other surface are collected on a lanoline treated body placed a short distance away. The sample is rejected if splinters are found adhering to the lanoline. Great difficulties were encountered during the development of safety goggles. The design even now is not settled. Flying goggles must be light and fit comfortably. They should not become fogged during the rapid changes in atmosphere frequently encountered at high altitude. The provision of a wide field of view is an essential requirement. It is important to provide protection against fire. Finally, the goggle must be of such shape as not to interfere with the fit of the flying helmet and oxygen mask. An idea of the work of development necessary in order to attain a satisfactory appliance is expressed in illustration (5) which from d to g shows some of the steps in design. The weight of goggle d was 7¾ ounces, while that of goggle g was 4 ounces. Not only is a heavy goggle uncomfortable to wear on the ground; but it is also far more handicapping in certain manoeuvres in flight. During a sharp pull out from a dive, the weight of a goggle may, for a few seconds, be increased by as much as fivefold and become displaced. As the weight factor is extremely important, an attempt was made to distribute pressures over the head from before backwards. The results shown at illustration (5), (a) proved unstable in wind. Masks such as (b) and (c) composed of synthetic material scratch too readily. Goggles of any form are not popular in aircraft with completely enclosed cabins, but are essential in some elementary training aircraft, and also in certain fighter aircraft, when the hood is moved to the open position for take off and landing. On occasions, a goggle has proved of value on abandoning the aircraft.

It has become necessary to provide safety spectacles of the type seen at (5), h, j and k. The spectacles are of two types, one intended for protection against glare (j), the other (k) for holding corrected lenses in the case of defective visual acuity. In order to provide a field of acute vision as wide as possible, it is necessary that the frames designed to hold correction fit close to the eyes. The lenses must be ground large. The measurements of the corrected safety lenses illustrated are 44×50 mm. It is also necessary to provide a type of fitting which will maintain the spectacles in position in the presence of strong wind. The side pieces, therefore, are of metal closely applied to the sides of the head. An alternative fitting is provided which permits an elastic strap to be attached to the outside of the flying helmet.

(*c*) Visors made of synthetic material have been a source of experiment. Two factors, however, militate against favourable

results; namely the softness of the substance, thus causing a reduction in visual acuity owing to the rapid appearance of multiple scratches and the difficulty in obtaining the material suitably tinted to ward off sun glare direct or reflected. It is also to be observed that the synthetic substances of the cellulose acetate group permit the unimpeded passage of ultra-violet light in contra-distinction to the properties of glass. The advantages of visors of this character are that they are light and can readily be moulded to fit the curves of the head and the contours of equipment. Visors are illustrated at (5) b and c, with tinted shields attached.

(*d*) The employment of contact lenses is limited by the intolerance from ocular sensitivity, of about 60 per cent. of those who undergo preliminary trials with the shells which are employed in the first instance. They are of great value in the few instances in which tolerance exceeds seven hours. They are strong and very resistant to fracture owing to the elasticity of the orbital content against which they are forced in the event of a blow.

(3) *Methods adopted to increase visual perception.*—An indirect but highly important method of aiding visual protection is to build up a system of instruction with the idea of quickening visual perception, thus raising the speed of detection and recognition of aircraft by day or night. The greatest attention has been

ILLUSTRATION 6.

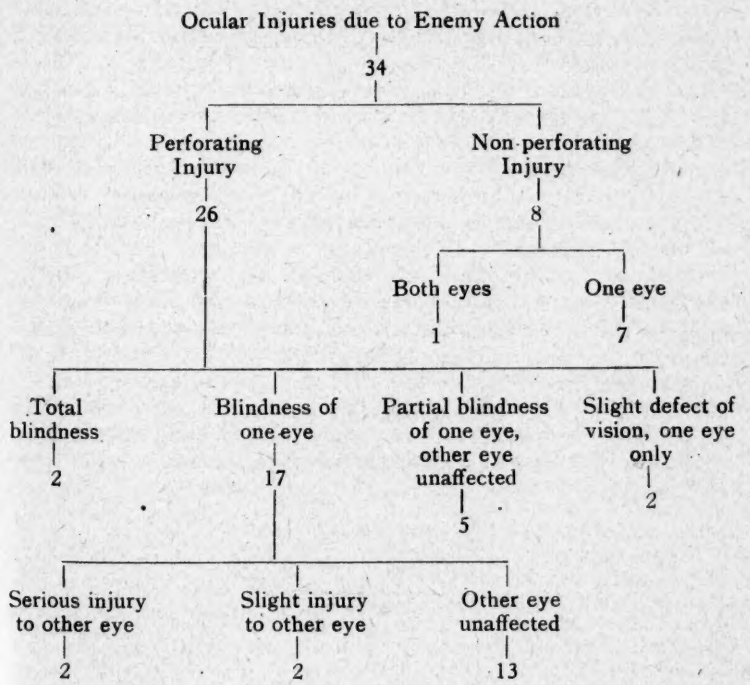
A gymnasium used for night vision training. Note the black and white painted hoops and skittles, as well as the white trestle used in walking and balancing exercises under low illumination.

given to improving performance under conditions of low illumination. The problem is complicated and the benefit gained is based largely upon assumption without clear statistical proof. The basis of this form of training received strong approval at Royal Air Force Headquarters, especially in Bomber Command. Fighter Command developed the technique in respect of its night fighter pilots. The aircraft were later equipped with radar for establishing contact with the enemy outside visual range. It was nevertheless essential for the human eye to establish identification. Night vision training comprises lectures upon the general principles of scanning at night time, together with practice using various devices under conditions equivalent to moonlight and starlight. Demonstrations are provided which show the effects created by altering the position of the source of night illumination upon ground targets. Games are played under low illumination in the gymnasium as illustrated in (6) with the participators wearing light trapped safety goggles containing dark filters. After a few lessons the improvement in performance is often remarkable. In the case of night interceptor pilots special care is taken to assure a high standard of night visual capacity before flying training in this branch of aerial warfare is commenced.

## The Assessment of Protective Measures

In estimating the full value of the measures which have been described, it is found very difficult to establish the position on a statistical footing. So many and varied are the situations encountered in War operations, that it is hard to discover sure ground from which the true value of visual protection can be calculated. For example, a number of personnel found it impossible to wear their goggles regardless of the wide field of vision provided and the eventual comfort attained, because they experienced a feeling of restriction, however good the optical qualities of the goggle glass. Much depends upon skill in the tactics of combat in the air which applies equally to both sides. Much of this skill is founded upon experience, with which goes a greater capacity for accurate and rapid visual perception. The element of fortune tends to exercise a strong influence upon the issue. It is, in truth, only possible to institute a search for various ways of protecting the eyes against injury, to employ every one that appears practical and likely to be appreciated, to spare no pains in explaining the value of these procedures, so that the greatest number of personnel will be encouraged to make use of them, and from this position to await the issue. One positive

approach in the campaign against blindness is the early elimination or treatment of those of doubtful visual capacity for day or night flying duties. At one time it was necessary to accept pilots with a visual acuity no better than 6/18 in both eyes correctable, however, at least to 6/6. To assist these personnel, over 12,000 goggles with correcting lenses were issued. The high standard of at least 6/6 in one eye and not worse than 6/9 in the other, was maintained for Air Gunners and Bomb Aimers. Over 200,000 tests for night visual capacity were carried out, with a rejection rate that rose to over 6 per cent. At the same time care was taken to observe personnel who were of borderline category in this respect, and have them sent to a special clinic if their performance in the air at night was adversely reported by the Captain of the aircraft. In this manner, in one year, over one hundred personnel were subjected to a careful examination in which the field of night vision was studied by means of self luminous targets, and eliminating action taken when field defects were discovered. Among such personnel were those who suffered from early retinal



disease, or from changes reflecting themselves in the scotopic visual field, as in diabetes.

## THE INCIDENCE OF BLINDNESS IN AIR CREW PERSONNEL IN FLIGHT

The total loss of sight of both eyes has occurred twice only in flying operations against the enemy. The after history of one case provides a fine example of the ability of youth to surmount this catastrophic event. Entering a University he studied law and obtained honours at the graduating examination. The policy which guides such cases into the care of the St. Dunstan's organisation is, without question, right. It is here alone that a full understanding of the psychology of blindness has been mastered.

The table, p. 699, provides an analysis of the ocular injuries from Royal Air Force records, confined to air engagements with the enemy.

## SUMMARY AND CONCLUSION

(1) The preservation of sight can be aided by the use of bullet proof glass screens and armour plates fitted within the structure of the aircraft.

(2) Further protection can be effected by equipping aircrew with flying goggles or spectacles fitted with safety glass windows which can be ground so as to provide correction in cases of refractive error, or by fitting contact lenses in certain cases in which the refractive error cannot be otherwise adequately treated. The eyes behind contact lenses can move over a wide range without loss of acuity.

(3) Visual training offers a valuable indirect method of protection by instructing personnel in careful scanning procedure, how to make the best use of rod vision under states of low illumination, and quickening the powers of recognition of the objects detected.

(4) The record of ocular injury sustained by personnel of the Royal Air Force in flying operations lends weight to the belief that a planned campaign against the hazard of loss of sight reaps its rewards.

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# GONIOTOMY FOR THE RELIEF OF CONGENITAL GLAUCOMA

BY

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SAN FRANCISCO

CONGENITAL or infantile glaucoma (hydrophthalmos, buphthalmos), has been among the most hopeless of ocular conditions requiring surgery. In the past, rare cases in which sight was preserved by operation or by spontaneous arrest appear to be exceptions that prove the rule. Trephination has been unsuccessful and often disastrous, cyclodialysis ineffective. A few cases of normalisation of pressure over a period of years by iridencleisis have been reported.

In recent articles[1, 2] observations on congenital glaucoma and the results obtained during the past ten years by goniotomy performed on 76 eyes presenting congenital glaucoma were published. In 66 of these pressure was normalised and vision maintained or restored. In ten the operation was unsuccessful.

Goniotomy is an operation for stripping or peeling embryonic tissue from the angle wall. If the cornea is clear the operation is performed under direct vision with the aid of a prismatic contact glass specially devised for this purpose. In this series the operation was performed under the contact glass on 20 eyes. On 56 eyes the operation was performed without the contact glass because of corneal cloudiness.*

It is the purpose of the present article to discuss the diagnosis and cause of reduced vision in infantile glaucoma and to stress the urgent need of early adequate operation. The technique of goniotomy is described. Indications for the operation and its mode of action, which are essential to an understanding of its principle, are set forth.

The operation is exacting. It requires teamwork and demands meticulous attention to detail of technique in order to obtain a high incidence of good results and to avoid injury which may have tragic consequences. Experience with gonioscopy and acquaintance with the varying picture of congenital glaucoma are helpful.

## DIAGNOSIS

The early symptoms in congenital or infantile glaucoma are often of a congestive and irritative nature. In the present series out of 87 eyes, 70 showed congestive symptoms at the time of onset.

* The approach to the angle across the chamber was first introduced by de Vincentiis in 1892 and some successes were reported. The method later fell into disuse.

Congestive symptoms caused by increased pressure consist of:

1. Corneal cloudiness, minor or extreme.
2. Hyperaemia of the bulbar conjunctiva, slight to moderate.
3. Photophobia, which may be extreme.
4. Epiphora.
5. Blepharospasm.

In 30 eyes cloudy cornea was present at birth. In 35 eyes the onset of congestive symptoms appeared between the first and fourth

FIG. 1.

(*Pre-operative*).—P.O'Q., aged 5 months, first seen July 25, 1944. Cloudy corneae developed six days before. Patient showed slight photophobia and tearing since birth. Pupils are in miosis due to three instillations of 5 per cent. solution of prostigmine every three hours.

FIG. 2

(*Post-operative*).—P.O'Q., aged 2½ years. From August 9, 1944, to October 2, 1945, four goniotomies were performed on each eye: The last operation on the right eye was nine months ago, and on the left eye eighteen months ago. Note clear corneae, normal-appearing eyes and complete absence of symptoms. Tension (McLean) March 17, 1946, was 34 mm. in the right eye and 34 mm. in the left eye without use of miotics. Refraction was −2.00 sphere in each eye. Ophthalmoscopic examination showed normal appearance of heads of optic nerves.

months. In 11 eyes the onset was between the fourth and ninth months. Some increase of pressure and enlargement of the eyeballs was present before congestive symptoms appeared, since these

children are often described as having had especially beautiful (*i.e.*, large) eyes. This appearance in otherwise normal looking eyes should arouse suspicion. Usually, however, the onset of congestive symptoms is the feature which calls attention

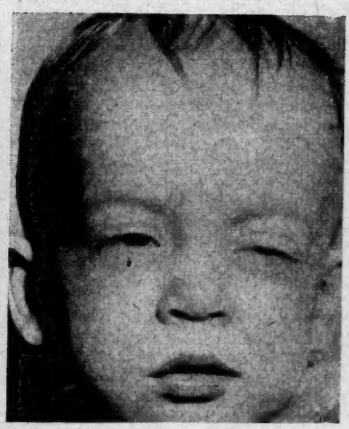

FIG. 3.

(*Pre-operative*).—T.C., aged 11 months, first seen July 10, 1942. Two months previously, on May 11, 1942, cornea of left eye became cloudy overnight. There were photophobia and tearing. The eye could be opened with difficulty; the bulbus was enlarged.

FIG. 4.

(*Post-operative*).—T.C., aged 14 months, three months after goniotomy was performed on the left eye, on August 21, 1942. Note clear cornea. The left eye is slightly enlarged, but is otherwise normal in appearance. On May 25, 1944, twenty-one months after the operation, tension (McLean) was 29 mm. in the right eye and 28 mm. in the left eye without use of miotics. Refraction was as follows: right eye, −1.00 sph. −1.00 cyl. axis 180°; left eye −3.50 sphere. Gonioscopy of the left eye showed stripping of angle in one-third of its circumference. Ophthalmoscopic examination showed wide shallow excavation of the head of the optic nerve of the left eye but no atrophy.

to the condition; the onset is often rapid and may be even sudden. Such was the case in six infants in this series in whom cloudiness of the cornea was discovered by the mother when the infant was taken up in the morning; the eyes had been clear the previous night. In one case the cloudiness was discovered when the infant was taken up from its afternoon nap.

The cloudiness of the cornea is often associated with photophobia, which may be so intense that the eyes cannot be opened except in the dark. For this reason it was impossible to obtain pre-operative photographs in many cases. Fig. 1 illustrates moderate cloudiness of the cornea. Fig. 2 shows the same patient

FIG. 5.

(*Pre-operative*).—J.V., aged 6 years. Since birth left eye was slightly larger and cloudy; there was some tearing. When first seen May 10, 1943, tension in right eye was normal, and in left eye was −1 to +2. Photograph shows patient avoiding light. There is some tearing.

FIG. 6.

(*Post-operative*).—J.V., aged 7 years. Goniotomy was performed on left eye May 12, 1943. Photograph shows patient one year after operation. Note clear cornea, absence of photophobia and normal appearance. Patient was last seen July 2, 1946, three years, two months after operation; excellent condition had been maintained; tension in right eye was 31, in left eye 33 (McLean), without miotics; media were clear; ophthalmoscopic examination showed wide shallow excavation of head of optic nerve not extending to the rim; colour of disc was good. Vision without correction, in right eye, is 0.8; in left eye, 0.4. With correction, vision in left eye is −0.50 sph. −0.75 cyl. axis 90°, = 0.6 and J.—2.

post-operatively. Figs. 3 and 5 illustrate pre-operative congestive signs of minor degree which permitted of photography. Figs. 4 and 6 show the same patients post-operatively. In the case of *T.M., aged 11 months, the eyes* were of normal appearance until the age of 6 months when, following whooping cough and pneumonia, *the mother noticed cloudy corneae.* From then on the child was

extremely photophobic. It spent its life playing at night in a dark room and sleeping during the day. When brought for examination it kept its head buried in its mother's bosom. A glimpse of the eyes could be obtained only by separation of the lids by force because of the intense blepharospasm. Ten days after goniotomy the corneae were clear and photophobia almost absent. Fig. 7

FIG. 7.

(*Post-operative*).—T.M., aged 11 months, first seen July 14, 1943. After whooping cough and pneumonia at the age of 6 months both corneae became cloudy and photophobia was extreme, so that the eyes could not be opened in daylight. Goniotomy was performed six months after the onset of symptoms, on the right eye on May 17 and on the left eye on May 20, 1943. Nine days after the operation the corneae were clear, eyes were open and patient tolerated light well. Eyes were normal in appearance, except for slightly increased size. There was no sign of corneal opacity, but retinoscopy showed slight irregular corneal astigmatism. There was myopia of approximately −2.00 sphere. On September 27, 1944 (sixteen months after the operation), tension (McLean) was 29 mm. in the right eye and 20 mm. in the left eye without miotics. In June, 1946 (three years after the operation) a letter from Texas reported patient's condition to be excellent to date.

shows this patient 16 months post-operatively. The corneae are clear; vision is excellent.

The corneal cloudiness and lack of lustre which is characteristic of the early stage was shown by staining with fluorescein to be due chiefly to a disturbance of the epithelium. It appears that it is largely this disturbance, consisting of roughening of the corneal

epithelium, which is the cause of the irritative symptoms and photophobia.

A physician who first sees the child with these congestive symptoms is apt to make a diagnosis of conjunctivitis, blepharitis or keratitis. He is not prone to think of glaucoma because the term "buphthalmos" is associated in his mind only with enlargement of the eyeball. The resulting delay in arriving at the correct diagnosis and instituting proper and adequate treatment may be tragic, for by the time the eyeball is strikingly enlarged the patient is usually well on his way to semi or total blindness. Therefore, in every case in infants in which irritative phenomena or corneal cloudiness are present, even though the bulbus does not appear enlarged, glaucoma must be suspected and intra-ocular pressure tested with a tonometer.

Tension should always be measured under ether anaesthesia which must be sufficient to assure complete relaxation at the moment of measurement. Other general anaesthetic agents have proved unsatisfactory. It has been found that tension may vary 10 to 15 mm. of mercury, depending on the depth of anaesthesia, and only when the patient was completely relaxed was the tension constant. Cases have been observed in which increased tension due to insufficient anaesthesia led to an incorrect diagnosis of congenital glaucoma. In the present series of cases in which the pressure was elevated, prostigmine 5 per cent. was instilled in the eyes every three hours and goniotomy performed as soon as possible.

In cases in which the cornea is sufficiently transparent one finds on careful gonioscopic examination characteristic evidence of congenital glaucoma in the chamber angle.

## CAUSE OF REDUCED VISION IN INFANTILE GLAUCOMA

Anderson[3] has pointed out that the cause of reduced vision in infantile glaucoma is usually regarded as being optic atrophy and one or more disorders in addition. In the present series atrophy of the optic nerve and others of these disorders were not the original cause, but were the result of progressive enlargement of the eyeballs and of tissue degeneration associated with the late, advanced stage of the disease. The primary cause of reduced vision in most cases in the series was a disturbance of the cornea. This disturbance begins with corneal cloudiness (oedema?). It appears to coincide with the onset of increased intra-ocular pressure. Allowed to persist it is followed by permanent scarring of the cornea with associated irregular astigmatism and ensuing amblyopia of greater or less degree. In those cases in which corneal cloudiness was relieved within a few days after onset acute vision developed.

## EFFECTS OF HYPERTENSION

(*a*) *Corneal cloudiness* is the main characteristic of the congestive phase of the early stage and at this stage is completely reversible surgically and occasionally by administration of miotics. The cloudiness usually occupies the central area. In severe cases it may cover the entire cornea, leaving only a strip adjoining the limbus clear. Fluorescein stains such corneae. Exposure to air, such as occurs when the blinking reflex is prevented while the patient is under general anaesthesia, increases the cloudiness and staining within a few seconds; if the lids are kept closed for a few minutes these decrease. That the corneal lesion is at least partially dependent on exposure is confirmed by its characteristic localization in the palpebral fissure zone. Abrasion of the epithelium in these cases shows a clear parenchyma in the denuded area. Another form of cloudiness appears in some cases to be due to an optical derangement of the corneal fibres. This cloudiness is evanescent. It can be produced by pressing on the bulbus; on relieving the pressure the cloudiness disappears.

The roughened epithelium appears to be the cause of the irritative symptoms which in turn are aggravated by exposure to air and by light. These irritative symptoms promptly disappeared following normalization of pressure, coincident with the simultaneous restoration of corneal lustre and epithelial integrity. Clinically the child's comfort closely paralleled the epithelial integrity. Patients presenting high intra-ocular pressure and good corneal lustre are usually comfortable and show no trace of photophobia or other irritative signs. Patients presenting lower pressure and poor corneal lustre display irritative symptoms. The tolerance of the cornea to increased pressure manifests great individual variation. In some cases in which the tension is 50 McLean the cornea may remain clear and irritative symptoms be absent during the course of many months; in others the development of the same degree of tension may immediately produce marked cloudiness and irritability.

Cloudiness of the corneae at this early age sometimes is associated with nystagmoid movements. In two cases these were relieved by clearing of the cornea. To illustrate: J.McL., born with cloudy corneae, presented marked nystagmoid movements when first seen at the age of five months. Three weeks after normalization of pressure in both eyes by goniotomy, these had greatly decreased. They disappeared almost entirely in the course of the next several months. In the case of J.H., aged three months when first examined, corneal cloudiness had developed two weeks previously. During the interval of 15 days which elapsed between

operation on the two eyes nystagmoid movements made their appearance. Two weeks after operation on the second eye when pressure was normalized and the corneae were clear, these disappeared.

Cloudiness of the cornea requires quick relief (1) because of the rapidity with which it interferes with the development of vision, and (2) because the longer it exists the denser and more extensive will be the ensuing permanent scar. The present series shows that corneal cloudiness can be relieved and that in most cases formation of a permanent corneal opacity and development of amblyopia can be prevented in great measure by early diagnosis and prompt operation.

(*b*) The cloudiness becomes a permanent scar. This " late " milky opacification develops from the original reversible congestive cloudiness of the cornea when the latter has lasted sufficiently long to cause permanent damage to the corneal parenchyma. The prolonged distention *per se* may also be a factor in its formation, or both factors may be operating concurrently. This type is reversible in part only. It involves chiefly the anterior layers of the corneal parenchyma. The epithelium shows normal to fair lustre and does not stain to fluorescein if the eye is in a non-congestive phase. Certain of these cases show relative absence of congestive symptoms because compensation has taken place. Pressure may actually be less than in the early stage, perhaps partially due to thinning of the tunics of the distended eye and possibly also to increased permeability of the occluding persistent meshwork in the angle resulting from stretching. The latter may be the mechanism, as has been suggested, which accounts for some of the rare cases of spontaneous arrest.

(*c*) *Amblyopia.* It is essential for the physician to keep in mind that a cloudy cornea during the first year of life, unless promptly relieved, retards the proper development of central vision at a most critical time. These cases illustrate the susceptibility of the development of visual function to normal entry of light through the refractive media in the first year of life. They stress the urgency of prompt and adequate surgical interference. They also show the need for diligent continued observation after pressure has been normalized, in order to detect beginning strabismus which could rapidly induce amblyopia unless proper treatment with complete occlusion of the fellow eye is instituted.

(*d*) *Glaucomatous atrophy of the optic nerve* was the exception in this series. It occurred only in those few cases in which normalization of pressure was unduly delayed. In the case of B.O'S. (Fig. 9), patient did not come to operation until the age of 4½ years. The left eye had been lost due to atrophy following a

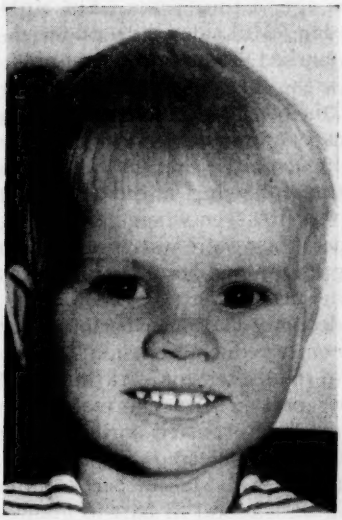

FIG. 8.

(*Post-operative*).—H.B., aged 7 months, when first seen on June 28, 1939. Three months previously the cornea of the left eye had become cloudy. Tension in the right eye was 20 mm. and in the left 90 mm. (McLean). Goniotomy was performed on the left eye on June 29, 1939. Drops of 5 per cent. solution of prostigmine were instilled every three hours in both eyes. On August 7, 1939, the tension (McLean) during ether anaesthesia was 50 mm. in the right eye and 31 mm. in the left. The cornea of the right eye was cloudy. Goniotomy was performed on the right eye. Three days after the operation the cornea of the right eye was clear. On November 27, 1939, three months after the operation the tension (McLean) in the right eye was 22 mm. and in the left was 22 mm. without miotics. On August 12, 1942, when the patient was aged 3 years 9 months, vision of the right eye without correction was 0.5 and of the left was 1/200. When the patient was last seen, on June 12, 1946, when he was aged 7 years and 7 months, his condition was the same, and the tension was normal. The right eye was emmetropic, the left eye myopic −3.50 sphere. The reduced vision of the left eye appeared to be due to amblyopia which developed during a transitory period of strabismus. Binocular fixation was present.

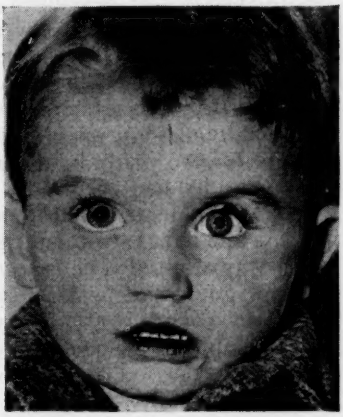

FIG. 9.

(*Post-operative*).—B.O'S., aged 4 years, first seen July 20, 1945. The left eye had been lost through trephine six months before. The cornea of the right eye was clear; tension (McLean) with miotics was 70 mm. Ophthalmoscopic examination showed glaucomatous excavation of the nerve head to the rim with slight pallor temporally. Vision was excellent, and visual fields were grossly normal. Goniotomy on the right eye with the contact glass was performed on October 12, 1945. Three months afterward tension (McLean) in the right eye was 26 mm. without miotics.

trephine operation performed at the age of four years. The right eye carried a pressure of 50 mm. Hg, McLean while under the influence of miotics. It showed marked glaucomatous cupping of the nerve-head to the rim. Because the cornea was clear excellent central vision had developed. This has been maintained since normalization of pressure by means of goniotomy performed one year ago. It is interesting to note, incidentally, that the excavation of the nerve-head almost disappeared following normalization of pressure. In the case of B.P., who was first seen when 5 weeks old, repeated goniotomy and other operations were unsuccessful on one eye for two years; by the time pressure had became normalized optic atrophy had occurred. In the case of L.L., aged 3 years, bilateral trephination with total iridectomy had been performed at the age of 8 months without permanently reducing tension. Cyclodiathermy also failed permanently to reduce tension. At the age of 3 years goniotomy was performed; pressure was normalized in both eyes, congestive symptoms which had persisted until this time were completely relieved and the corneae cleared considerably. Moderate reduction of vision was found to be due in part to faint corneal scarring with irregular astigmatism and in part to glaucomatous atrophy which had occurred as a result of the protracted period of time during which the pressure remained elevated.

Ruptures or tears of Descemet's membrane, which are prominently referred to in the literature describing the pathological anatomy of " buphthalmos," were absent in this series of infantile glaucoma. It appears that tears of Descemet's membrane in infantile glaucoma do not occur before marked distension and degenerative changes have taken place. These conditions did not exist at the time goniotomy was performed in this series, which probably accounts for the absence of tears. If this observation is correct, rupture of Descemet's membrane plays no rôle in diagnosis at the time when diagnosis is of therapeutic importance.

## MODE OF ACTION OF GONIOTOMY

In congenital glaucoma the angle presents a characteristic gonioscopic appearance which shows little individual variation. Other anomalies such as gross anterior adhesions were present in only 2 out of 77 eyes examined by the writer. The characteristic condition appears to consist of an abnormal insertion of the iris, by means of adventitious mesoblastic tissue into the angle wall anterior to its place of normal insertion.* Gonioscopic examination

* Gonioscopy of normal eyes of infants indicates that the chamber angle does not assume adult appearance until after the age of several months indicating that the uveal meshwork continues to regress after birth. This appearance can in most cases be distinguished from the pathological persistence of uveal tissue which is present in congenital glaucoma.

with hand slit-lamp and binocular microscope held in the hand reveals that the iris continues in a horizontal plane until it reaches the posterior surface of the cornea. This is in contrast to dipping backwards of the iris as seen in the adult, thus forming a sinus or the so-called chamber angle. The point of attachment corresponds to the position of the anterior border ring of Schwalbe. The area of transition from the anterior surface of the iris to the posterior surface of the cornea consists of a gelatinous looking semi-transparent substance. This area may be so narrow that it barely constitutes a line. It may be wider, in which case the beam of light shows the tissue to be in a plane anterior or axial to the true angle

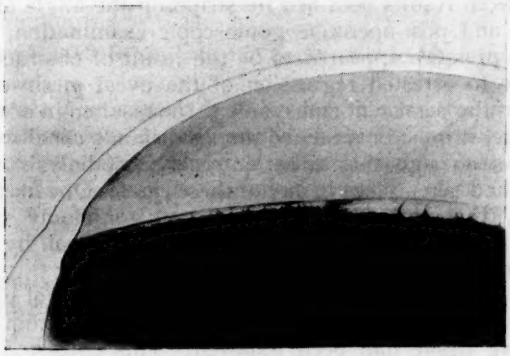

FIG. 10.

Drawing shows post-operative microgonioscopic appearance at the point of transition between the area on the right in which the angle has been stripped and the neighbouring untouched region.

wall the presence of which can in some cases be discerned in a deeper plane. Delicate arborescences of uveal meshwork which cross the angle can be seen resting on the semi-transparent substance which fills the angle behind them. From this finding and from the flare of the beam of the slit-lamp traversing it, it is evident that the angle is not an optically empty space. This fact becomes especially evident post-operatively at the point of transition between the area in which the angle has been stripped and the neighbouring untouched region (Fig. 10). The gonioscopic appearance corresponds to that which would be expected from a study of histological sections of eyes affected with congenital glaucoma enucleated in the early stages. Post-operative gonioscopy in the successful cases revealed that the procedure had been effective in stripping the persistent embryonic tissue that obstructed the filtration angle over

an area from one-fourth to one-third of its circumference. Figure 10 shows a case in which stripping successfully normalized pressure. Analysis of this series of cases suggests that stripping of this amount of the angle is sufficient and is the *sine qua non* of successful normalization of pressure. It also suggests that stripping of only a part of the circumference is adequate to permit the pressure regulating mechanism to assert itself and permanently to maintain normal tension and function. Since this effect has been observed in individual cases as long as 10 years after goniotomy, and since cases of recurrence of increased pressure have been the exception, it appears that the effect is permanent.

In all bilateral cases in this series and in most monocular cases, judging from results obtained by stripping the angle and by pre-operative and post-operative gonioscopic examination, the initial increased pressure appeared to be the result of obstruction of the angle due to arrested regression of the uveal meshwork. Since removal of the persistent embryonic tissue resulted in normalization of pressure, it must be assumed that Schlemm's canal was present. There was no sign that either internal cyclodialysis or external filtration had taken place in any of these cases. One may conclude, therefore, that the mode of action of goniotomy consists in restoring access of aqueous to Schlemm's canal by removing obstructing tissue.

In one case there was direct gonioscopic evidence of the presence of Schlemm's canal in that portion of the angle from which the obstructing tissue had been removed. This consisted of a pink band which was seen to lie external to the trabeculum in the position of Schlemm's canal. In the adult this pink band has been shown by Kronfeld to be produced by blood in Schlemm's canal[4]. The presence of Schlemm's canal is suggested by the post-operative gonioscopic findings in the aforementioned successful cases. It is confirmed by the analysis of anatomical examination of 84 specimens taken from unoperated eyes, as reported by Anderson[5]. He found that Schlemm's canal was present in 75 per cent. of the earliest specimens. No sign of it was found in more than half the specimens taken from children over 2½ years of age. He suggests that the canal becomes closed in the later stages as the result of distension of the eyeball and of increased intra-ocular pressure. The evidence obtained from these specimens thus confirms the rationale based on gonioscopic examination of the effectiveness of stripping the angle in early congenital glaucoma.

## URGENT NEED FOR EARLY OPERATION

The mode of action of the operation as explained in the foregoing shows the importance of early diagnosis for a successful

outcome of operation, and explains why the chances of establishing outflow with this operation may be expected to diminish with the duration of the condition. It is essential to operate early before prolonged distension of the eyeball has caused obliteration of Schlemm's canal. Other important reasons for early diagnosis and prompt operation are:

1. Restoration of vision by means of clearing the cornea. Corneal cloudiness is largely reversible in the early stages, progressively less so in later stages.

2. Prevention of amblyopia due to prolonged obstruction of vision by cloudiness of the cornea.

3. Prevention of permanent scar formation developing from corneal cloudiness.

4. Prevention of injury to the optic nerve caused by prolonged pressure.

In general, it is important to prevent progressive enlargement of the eyeball before distension has produced permanent changes and to encourage development of normal anatomy and of physiological function during the period of growth.

## RESULTS

The results of goniotomy* in congenital glaucoma are summarized in the following tabulation:—

TABLE I

*Goniotomy in Congenital Glaucoma*

| | |
|---|---|
| Number of infants and children ... ... ... ... | 51 |
| Eyes operated on by goniotomy ... ... ... ... | 76 |
| Successful (pressure normalized; vision maintained or restored) ... ... ... ... ... ... | 66 |
| Unsuccessful ... ... ... ... ... ... | 10 |
| Eyes on which goniotomy was not applicable ... ... | 11 |

It has been my custom to prescribe miotics three times daily for two months after surgery. The result of the operation was considered successful when intra-ocular pressure never rose higher

* Goniotomy in infants and in adults is two distinct operations which differ in rationale, technique and effectivity. In infants the operation, which has been developed to a relatively satisfactory conclusion, consists of removing occluding foetal meshwork from the angle. In adults, in whom it has not yet shown an adequate degree of consistent efficacy to recommend its employment except in the occasional case, its objective is to incise the angle wall, that is the trabeculum proper. For this reason it is suggested that the term goniotomy be applied only to the operation performed on infants, and goniotrabeculotomy or trabeculotomy to the procedure carried out on adults.

than 35 mm. of mercury with the McLean or 21 mm. with the Schiötz tonometer three months after operation, no miotics having been used during the two weeks preceding measurement of the pressure.

Among the successful cases the time elapsed since the date of operation varied from six months to ten years. There were recurrences in two eyes, mentioned in the next paragraph. The oldest case (two eyes) was operated on ten years ago; 5 eyes seven years ago; 8 eyes six years ago; 21 eyes from four to six years ago; 11 eyes from two to four years ago; 9 eyes from one to two years ago and 10 eyes from three to twelve months ago.

The recurrence of increased pressure which took place in two eyes was relieved by a second goniotomy in both instances. In F.W. pressure increased in the left eye eight years after operation. In J. McL., pressure increased in the left eye four years after operation. Gonioscopic examination showed that the stripping of the angle had been insufficient.

Repeated operations were necessary in 22 eyes before pressure was permanently normalized. One operation sufficed in each of 45 eyes. In some cases, for example that of P.O'Q. (Fig. 1), goniotomy was performed four times on each eye before permanent normalization was attained. The ultimate result was excellent. I believe it is better to err on the conservative side and partially strip the angle with safety on repeated occasions than to attempt to do an extensive stripping at one operation at the cost of greater hazard. Cases which required repeated operations before permanent normalization was attained are not listed as recurrences.

The operation was performed under the contact glass on 20 eyes. *All of these were successful. Repeated operation is the exception when operating under the contact glass.* In 56 eyes the operation was performed without the contact glass because of corneal cloudiness. On 18 of these repeated operation was necessary.

In 8 eyes which had been ineffectively trephined goniotomy normalized tension.

## ADVANTAGES, DISADVANTAGES AND HAZARDS

Striking among the results of goniotomy are absence of cosmetic disfigurement and preservation of a round central freely reacting pupil.

A disadvantageous feature of the operation without the glass is the need to repeat the operation in one-third of the cases in order to obtain permanent normalization of tension.

Hazards of the operation are excessive haemorrhage or iridodialysis if the root of the iris is incised. Vision was lost in two

eyes early in this series as the result of excessive haemorrhage. Recently one eye in a congestive neglected case of a 2½ year old child was lost as the result of a massive intra-ocular haemorrhage which occurred on the sixth post-operative day. Infection, as in any other intra-ocular operation, is a possible complication but was not encountered in this series. A severe reaction occurred in one case which could be considered an infective iritis. As always the eyes had been operated on different days, in this instance after an interval of three weeks. The condition cleared after 18 days leaving in one eye a small central opacity of the anterior capsule; in the other an anterior adhesion produced eccentricity of the pupil. Tension was normalized and it is evident that useful vision is developing. Sympathetic ophthalmia has occurred in no case up to the present time.

## INDICATIONS

Goniotomy is indicated in all bilateral and unilateral cases of congenital glaucoma in which increased pressure is the result of obstruction of the angle by persistent embryonic tissue, provided that Schlemm's canal has not been obliterated by prolonged distension of the bulbus. This includes the majority of cases of congenital glaucoma in the early stages. Generally speaking, the earlier it is applied after onset of symptoms the more effective is the operation in maintaining and restoring vision. Results may be dramatic when the bulbus is in the early congestive phase associated with cloudiness of the cornea. In these cases the urgent need for early diagnosis and prompt adequate operation can hardly be over-emphasized. There are cases, however, which run a chronic course during which the corneae remain clear, the optic nerve undergoes little damage and the bulbus is only moderately enlarged after a long period of time. Good central vision is maintained in them. Since the corneae are clear goniotomy can be performed under direct vision with the aid of the glass, and may be effective several years after the onset of symptoms. Excellent results were obtained in some of these cases at 4 and 6 years of age with corneal diameters of 14 mm.

## CONTRA-INDICATIONS

Goniotomy is contra-indicated in older children with enlarged eyes, that is, in eyes in the advanced stage which have had a congestive history with consequent corneal scarring and cloudiness and a corneal diameter of 15 mm. or more. In these enlarged "buphthalmic" bulbi the danger of haemorrhage is greatly

increased because of dilated vessels and collateral circulation which has become established. Haemorrhage is absorbed more slowly, no doubt due to degenerative condition of the eyes and to their changed circulation. Schlemm's canal may be obliterated as a result of the distension.

When permanent obliteration of the canal has taken place and when repeated goniotomies have proved ineffective, iridencleisis or cyclodiathermy may be tried.

Some rare unilateral cases of congenital glaucoma appear to be the result of other kinds of anomalies, such as an aberrant reflection of the iris stroma to an insertion at the anterior border ring. The extremely rare cases of narrow angle (angle or iris-block) glaucoma[6,7] in small children do not come within the scope of this article since goniotomy is not applicable to them.

## TECHNIQUE

There are two major procedures of goniotomy: if the cornea is clear goniotomy is performed by direct vision under a prismatic contact glass; if the cornea is cloudy it is done without the glass. The general considerations which the procedures have in common will be treated first.

### GENERAL CONSIDERATIONS

*Pre-operative measures.* Paediatric examination including X-ray of the chest for enlarged thymus is performed in all cases. In the case of infants, the usual diet is maintained up to 6 hours pre-operatively; sugar solution is forced up to 4 hours pre-operatively to avoid dehydration with associated hyperpyrexia. In order that surgery may not be delayed and since ether may have to be given several times in the course of the following weeks, every effort should be made to prevent the infant from catching cold. Miotics, preferably prostigmine 5 per cent., are continued usually every 3 hours while the patient is awake until 1½ hours before the time of operation. One extra drop is instilled three times at intervals of half hours before operation in the eye to be operated upon. If circumstances permit one drop of sulmefrin is instilled t.i.d. for several days pre-operatively.

*Anaesthesia.* In view of the delicacy of the operation as applied to infants, which may be only a few days or weeks old, anaesthesia is an important factor. A preliminary injection of atropine is given 45 minutes pre-operatively. Ether is administered through a small airway (intrapharyngeal insufflation). A generous supply of oxygen should be assured at all times. While the patient is being

prepared the lids must be kept closed with moist pledgets but without pressure, since the cornea in congenital glaucoma is extremely susceptible to exposure and to pressure. For the same reason the heat generated by operating room lamps should be avoided. Anaesthesia must be sufficient at the moment of operation in order that there be no movement of the patient. In children over six months of age a small dose of paraldehyde is administered rectally 45 minutes pre-operatively. Post-operative agitation which may follow ether anaesthesia is not harmful since there is only a small obliquely placed puncture wound which does not permit egress of ocular contents. Before the patient is draped pressure is taken with a tonometer, the base of which has been sterilized. The corneal diameters are measured, and the condition of the cornea and size of the pupils noted. Sometimes the decision of which eye to operate upon can be made only at this time.* Then the position of the patient, operator, assistant, anaesthetist and instrument table is arranged accordingly.

*Position of Patient.* The infant is placed on a circumcision board : for the right eye on the centre of the operating table ; for the left eye with the head end of the board protruding obliquely off the table. For operation under the glass the eye should be 47 inches above the floor to permit a convenient position for an operator 5 feet 10 inches in height. For goniotomy without the glass the patient's eye should be 46 inches or less above the floor in order that the operator may look vertically down upon it. A pillow or towels are placed under the head bringing it into a horizontal plane. The anaesthetist maintains the head in position during the operation.

*Position of Operator and his Assistants.* The operator stands on the side of the eye to be operated on : for the right eye at 11 o'clock ; for the left eye, at 4 o'clock. The illuminator holding a hammer lamp must be high enough, standing on a platform if necessary, to obtain a good view of the field of operation. He stands on the same side and to the right of the surgeon for the operation with the glass, on the opposite side for operation without the glass. The assistant fixates the bulbus with two Gifford forceps with lock, standing at 3 o'clock for the right eye and behind the head for the left eye. The anaesthetist is on the side opposite the operator, for the right eye at 5 o'clock in order not to interfere with the assistant who is standing at 3 o'clock.

*Magnification.* The operator uses a +2·50 sphere hanger over his correction. He wears a binocular head loupe +5·00 sphere

* In cases in which the decision has already been made the taking of the tension is dispensed with as a preliminary procedure in order to reduce the time of anaesthesia.

(Hess head loupe) which he uses only in case the anterior chamber is deepened through a corneal puncture made with a discission knife. He does not use it for the goniotomy.

*Illumination.* The room is in semi-darkness. One lamp situated at some distance from the table and directed away from it is in readiness for general utility purposes. The field of operation is

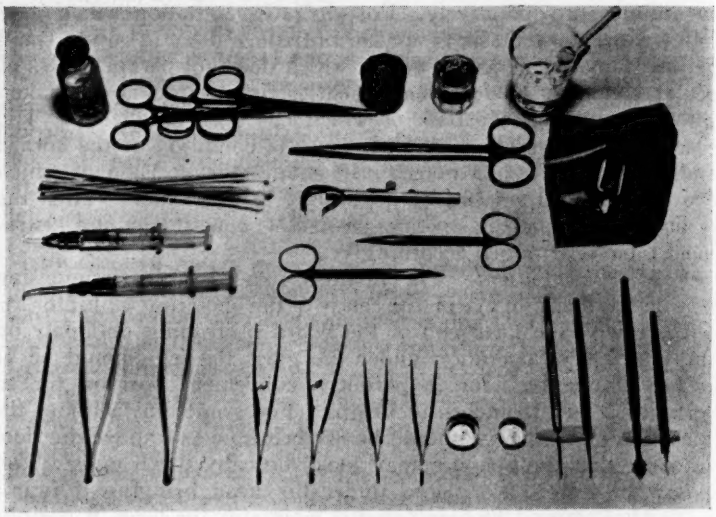

FIG. 11

Usual set-up tray for Goniotomy. Ampoule of physiological saline. Haemostats, mosquito. Dappen glass containing tincture of iodine. Dappen glass containing solution fluorescein, 1 per cent. Medicine glass containing physiological saline and glass rod. Speculum with rubber dam. Applicators. Mayo scissors. Luer-Lok syringe, 2 c.c. with ½ 30 needle, containing physiological saline solution.—Caliper. Stevens' scissors. Lacrimal dilator. Splinter forceps. Gifford's forceps with lock. Bishop-Harman's forceps. Surgical contact glass (small and large). Goniotomy knives. Keratome. Discission knife, narrow.

illuminated by a hammer lamp* which is made of light plastic and is air cooled. It is used in both procedures but manipulation differs respectively. The illuminator must be familiar with and trained in the procedure. The technique of illumination is especially important in goniotomy by direct vision under the glass and must be carefully rehearsed before the operation.

*Instrument tables.* Small and large instrument tables are on the side of the eye to be operated upon (Fig. 11).

* This lamp was demonstrated at the meeting of the A.M.A. in San Francisco, July 4, 1946 A description of it is in publication.

*Preparation of Patient.* Lashes are clipped (with Stevens' scissors and ointment, wiped off with cotton spindle after each clip). The face is prepared and the eye irrigated in the usual manner. After the patient is draped a face mask, which should be of moistened gauze in order to be easily moulded to the region, is applied.

## GONIOTOMY UNDER THE CONTACT GLASS

Once the glass has been applied, time is the essence of goniotomy. A complete check, therefore, is made beforehand in order to assure that everything is in readiness and in position on the instrument table. The speculum is passed through two holes made in a piece of rubber dam 6 inches square. The height of the assistant and of the illuminator is checked. Either or both may require a platform to stand on. The lids are kept closed throughout the preparation. A few minims of adrenalin 1 : 1000 are injected with a #30 needle and 1·5 c.c. Luer syringe into the outer canthus; after one minute a canthotomy is performed with straight Mayo scissors. The quartz surgical contact glass which has been cold sterilized is dried and placed on gauze in a small bowl on the instrument table. The knives (2 goniotomy and 2 discission knives) are now placed on the table, points toward the operator.

The operator stands at 11 o'clock for the right eye and at 4 o'clock for the left eye. The platform upon which the illuminator is about to stand is already in position to the operator's right. The instrument table and surgical nurse are also to the right of the operator. The speculum is now inserted and the rubber dam trimmed especially on the nasal side. On the temporal side the dam covers the lids, preventing contact of the knife with them and relieving the operator's mind of this important detail. The cornea is moistened when necessary with physiological saline solution applied by means of a glass rod. The eye is fixated by the assistant 2 to 3 mm. posterior to the corneo-scleral border at 12 and 6 o'clock by means of two Gifford forceps with spring lock. He must be mindful not to touch the lock lest it spring open during the operation. The head and eye are rotated away from the surgeon who applies the contact glass in the usual manner by injecting physiological saline solution between it and cornea through a Becton, Dickinson curved gold canula and 1·5 c.c. Luer syringe.

When operating on the right eye (Fig. 12) the fixator's right hand holds the forceps at 12 o'clock, the left at 6. The left hand must be in such a position that it does not obstruct the view of the illuminator as he moves counter-clockwise. When operating on the left eye, the right hand is at 6 o'clock and the left at 12.

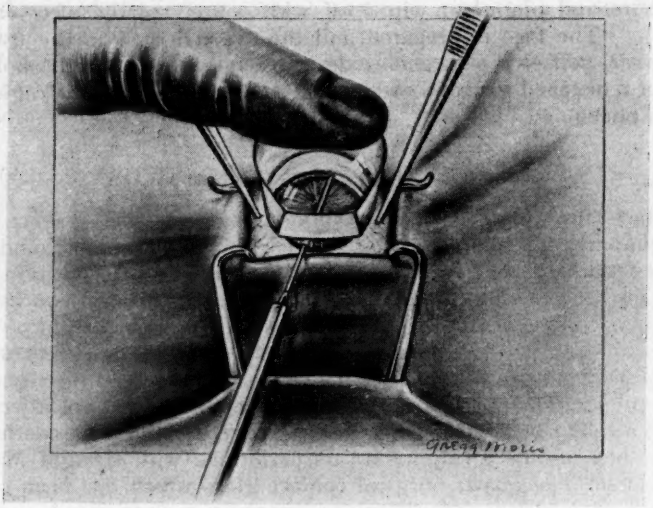

FIG. 12

Drawing shows goniotomy or stripping of the angle under the glass. The root of the iris retracts behind the blade, leaving a white wake behind it which is the wall of the angle.

Regardless of the side under operation, the fixator, unless tall, should stand on a platform in order to assure visibility of the eye throughout the procedure and to prevent the tendency arising from poor visibility to retract or dimple with the forceps. The surgeon supports the glass with the index finger of his left hand. Two indentations on top of the glass prevent the finger from slipping. The fixator abducts the eye slightly in order to expose a strip of the temporal portion of the cornea 2 or 3 mm. wide where the puncture is about to be made. By abduction the eye can be made to offer resistance to the glass when this is pressed more firmly against it by the operator's finger at the moment of puncture, thus preventing ingress of air at this critical moment. The operator applies the end of a cotton applicator previously dipped in tincture of iodine at the intended site of puncture. The goniotomy knife is then passed to him by the instrument nurse. She retracts the instrument table and the illuminator assumes his position on the platform immediately to the operator's right.

The illuminator stands on the platform sufficiently far removed from the surgeon to provide room for him to sway counter-

clockwise during the progress of the incision. The illuminator must stand with feet well apart in order to be able to sway in unison with the counter-clockwise movement of the surgeon without having to take a step. He maintains the lamp in contact with the temple of the surgeon, at the same time looking down the top of the shaft of the lamp, so that he may have the same view of the angle and of the blade of the knife as the surgeon. The heads should maintain contact. Perfect synchronization of heads and light is necessary; they must move as one unit. A light on a head band did not give as good results as the technique described.

The eye first having been rotated 2 hours counter-clockwise puncture is made in the right eye at 10 o'clock, in the left at 4 o'clock, 1 mm. anterior or axial to the corneo-scleral border and oblique so that the corneal wound is valve or trapdoor-like. At the moment of puncture, extra pressure is exerted by the operator's index finger on the glass in order to prevent ingress of air. Pressure must be exerted in the direction of the optic axis as tilting of the glass permits entrance of air. For the same reason dimpling of the sclera with the fixator's forceps must be avoided. The operator guides the knife across the pupil to the opposite side. In traversing the chamber the knife must always cross the optic axis. When the knife crosses the optic axis the diameter of the arc described after the opposite angle is engaged will be greater than the diameter of the circumference of the limbus. Therefore, the point of the knife remains engaged. When the knife does not cross the optic axis, the contrary holds true. In describing a smaller arc than that of the limbus, the point of the knife becomes disengaged and too small an incision is made. Moreover, the extra movement of advancing the knife necessary to maintain contact with the angle wall is prone to result in picking up iris tissue near the root with consequent iridodialysis and haemorrhage. The blade is inserted just anterior to the root of the iris and is moved counter-clockwise in this plane as long as visibility permits. This usually amounts to several millimetres or from one-fourth to one-third the circumference. During this excursion of the blade, the shaft is rotated around its axis in a clockwise direction to encourage a stripping action and to prevent the blade from moving posteriorly out of the intended plane into the dangerous region of the ciliary body. During stripping under the glass, the root of the iris is seen to retract behind the blade, leaving a white wake behind it which is the wall of the angle. In some cases this has the appearance of a cut piece of parchment paper that drops backward as the incision proceeds. Stripping should be under complete control and placed immediately above the root of the iris, care being exercised to avoid blood vessels at the iris root which in some cases

are clearly visible. There may be a slight sensation of grating as the blade proceeds; the fixator may recognize the need of exerting slight resistance. Since picking up the root of the iris causes haemorrhage it is advisable to start well anterior to the root and to strip or peel off the insertion of the iris from above. When stripping has been completed the knife is quickly removed, without loss of aqueous in most cases, care being taken to avoid enlarging the puncture wound in the cornea by slight pressure against the back of the blade during its removal. The contact glass and fixating forceps are withdrawn. After a few seconds a slight oozing of blood of venous colour appears in the anterior chamber along the line of stripping; this is absorbed within a few hours. If after removal of the knife the pupil should be eccentric, the cornea is tapped near the puncture with a spatula or the tip of a lacrimal dilator is inserted to prevent adhesion of iris to the inner wound lip.

The speculum is removed and the canthotomy closed with catgut. Eserine ointment 1 per cent, and sulphathiazole ointment 10 per cent. are inserted into the conjunctival sac. Binocular pads are applied, that over the operated eye being covered by a metal shield. The child is placed in bed on the operated side in order that any blood may settle on the opposite side of the chamber. Arm cuffs are applied. In older children, restrainers may be necessary. Elixir phenobarbital dram 1 may be indicated. After 24 hours it has been customary in bilateral glaucoma to instil prostigmine 5 per cent. in the unoperated eye and after 48 hours in the operated eye; thereafter drops are continued three times a day in both eyes. Only one eye is operated on at a time.

If the different steps of the procedure have been reviewed preoperatively there should be no loss of time at operation so that once the glass is applied goniotomy is quickly completed.

If goniotomy under the glass is not feasible, the operation is performed without the glass. Operating under the contact glass is desirable whenever possible. In the past various procedures (use of glycerin, hypertonic salt solution, retrobulbar injection of adrenalin 1 :1000 *inter al.*) have been tried without success with a view of clearing a cornea which has become cloudy during pre-operative manoeuvres, application of forceps and glass. Letting off a small amount of aqueous through a valve-like corneal puncture made with a Graefe knife was also tried. It cleared the cornea but did not permit of adequate operation under the glass because of complicating circumstances. *Recently a preliminary operative abrasion of the epithelium prior to application of the contact glass has enabled operation under the glass in cases in which it has heretofore been impossible.*

## GONIOTOMY WITHOUT THE CONTACT GLASS

The preparatory measures already outlined for goniotomy under the glass are carried out. The precautions mentioned under general consideration are observed. The height of the eye should be such that the operator looks vertically down upon it. Illumination is provided by the hammer lamp carried on the end of a rod so that the light falls as nearly vertically from above as possible. The illuminator stands opposite the surgeon, for the right eye at 4 o'clock and for the left eye at 10 o'clock. The rubber dam on the nasal side must be trimmed well back to avoid casting a shadow on the field of operation. The bulbus is fixated with two forceps held by the assistant, in the same manner as for the operation under the glass. The forceps should be vertical to the sclera and must include episcleral fibres in order to permit of resistance or counter-pressure on the part of the fixator during stripping. Additional fixation by the operator with a Bishop Harman forceps held in his left hand is helpful. If the assistant is not sufficiently experienced with this operation, it is best to divide the fixation between him and the surgeon. In this case the surgeon fixates with the Gifford forceps with lock in his left hand at 12 o'clock on the right eye and at 6 o'clock on the left, while the assistant fixates with his left hand at 6 o'clock on the right eye and at 12 o'clock on the left.

Canthotomy is indicated in most cases. In small infants, on whom the operation is especially delicate, the head is rotated toward the surgeon and the eye slightly abducted in order to bring the nasal limbus into a frontal plane to the surgeon's line of regard. In the case of a greatly enlarged eye this lateral movement is limited because the temporal limbus disappears as the result of even slight abduction. The surgeon applies Bishop Harman forceps at the contra-lateral limbus, helping to fixate and guide the rotation from there.

The puncture in the cornea is made as already described, being sure that it is oblique (valve-like) in order to encourage retention and reformation of the anterior chamber. It is made on the right eye at 10 o'clock, the eye having first been rotated counter-clockwise 2 hours. The blade of the knife crosses the pupil and disappears behind the limbus on the opposite side in a plane just anterior to that of the iris. As it engages the angle wall and starts its excursion in a counter-clockwise direction slight resistance is felt. Its tip can be seen through the sclera from the outside. Seen through the cornea, the knife appears 0·5 mm. farther anterior than it is in actuality. This appearance must not influence the surgeon to guide his knife farther posteriorly. A posterior position

of the blade is the greatest hazard of the operation. It is better to err on the conservative side by maintaining a more anterior plane at the risk of not stripping the angle. The operation can always be repeated. Rotation of the knife clockwise around its own axis helps to prevent it from being guided or from slipping to a posterior position. Stripping the angle wall is usually associated with a feeling of slight resistance and of grating if the blade is not too sharp. The absence of this feeling is an indication that the blade is too far posterior and must be avoided. If indicated the knife may be reversed and the stripping repeated in the opposite direction.

If upon re-examination later this goniotomy proves to have been insufficient, another can be performed on an adjoining part of the angle after suitable rotation of the eyeball. It has been possible in some cases, as shown by post-operative gonioscopy, to strip the angle over almost one-half its circumference at one sitting. Picking up the root of the iris and haemorrhage are the only serious complications to be guarded against. It has been found that removal of blood from the anterior chamber by paracentesis and irrigation cannot be adequately accomplished in infants. It is better to be obliged to repeat the operation than to provoke a major haemorrhage by too posterior position of the blade or by attempting too extensive stripping. If the stripping has been properly placed a little blood of venous colour begins to ooze from several points along the line of stripping a few seconds after removal of the knife. If the head is rotated to the opposite side, the blood coalesces to a thin sheet in the region of the pupil and is seen to stop. If the blood is more arterial in colour, is more extensive and follows immediately upon the incision, it is an indication that the latter has been placed more posterior than is desirable. Blood may fill one-half the chamber; it is usually absorbed within 24 to 48 hours.

The canthotomy wound is sutured, medications given and dressing applied as already outlined in the procedure under the glass.

*Notes on Stripping of the Angle.* In congenital glaucoma, there is an area of from 2 to 3 hours in the circumference of the angle opposite the point of puncture in which it is easiest to make an adequate stripping. Since the position of the puncture is limited on the right eye by the brow and on the left by the cheek bone, a point is chosen as far as possible in a clockwise direction—for instance, on the right eye at 10.30 o'clock in order to strike the opposite nasal angle as far clockwise as possible, *i.e.*, 4.30 o'clock. When the blade has reached 2.30 o'clock it has covered the area in which stripping can be done under optimum conditions and with least hazard. Post-operative gonioscopy shows that it is often possible

to strip a more extensive area, up to 4 hours or more by the clock. Since this cannot be done consistently and since it is associated with greater hazard of haemorrhage, it is well to consider allocating the area of the first stripping in such a way that another area of the angle as yet untouched can be stripped on a second occasion. For this purpose it is advisable in both procedures, with and without the glass, to start with the eye rotated 2 hours in a counter-clockwise direction. Thus for operation on the right eye the bulbus is rotated in a counter-clockwise direction so as to bring the area between 6 and 3 of the nasal angle within operative reach. The assistant maintains the bulbus in this position and resists, if necessary, the traction of the blade while it strips the angle in a counter-clockwise direction. If later examination shows that the result of this procedure was not sufficient to normalize pressure, stripping of a neighbouring area of the angle (from 3 to 12) may be undertaken. In the latter case the right eye is rotated two hours in a clockwise direction to make the area accessible. The puncture is made at 10·30 o'clock and stripping is performed from 5 to 3 o'clock in the rotated position which corresponds to 3 to 1 o'clock when the bulbus is in the normal position. It is possible, therefore, by means of two goniotomies to strip the angle up to one-half its circumference, *i.e.*, from the 6 to 12 meridians.

*Preliminary Deepening of the Anterior Chamber with Physiological Saline Solution.* Preliminary deepening of the anterior chamber with physiological saline solution may be performed in cases operated on without the glass in order to minimize the hazard of picking up the root of the iris with the tip of the knife. The chamber is not deepened for the operation under the glass; in this case the blade of the knife is guided under direct vision and therefore picking up of the iris root with consequent haemorrhage can be avoided. Deepening should be considered in infants, especially those between the ages of several days to weeks because of the relatively shallow chamber and narrower angle. It permits of a more deliberate placement of the stripping in regard to its antero-posterior position. However, it is well to dispense with deepening when possible as it introduces a delicate technical detail which, if not adequately performed, may result in leakage of aqueous and postponement of the operation. When deepening is employed great care must be taken in prelaying the corneal puncture. The bulbus is fixed with a Bishop Harman forceps at the opposite limbus. The cornea is punctured very tangentially 1 mm. axial to the corneo-scleral border at 9 o'clock on the right eye and at 3 o'clock on the left eye, with a discission knife, the blade of which has been previously dipped in fluorescein. The wound canal should

be at least 3 mm. long. The tip of the knife should barely perforate Descemet's membrane as observed through a five times magnifying head loupe. It may be necessary to tip the knife backward a little in order to perforate this membrane. Care must be taken not to enlarge the puncture upon removing the discission knife lest leakage ensue. The puncture made visible by fluorescein is touched with a dry applicator and one dipped in tincture of iodine from which the excess has been removed. With a #30 needle (previously drum tested or examined under a loupe to assure its having a perfect point) attached to a 1·5 c.c. Luer syringe intravenous saline solution is injected, the surgeon fixing the bulbus at the contra-lateral limbus with a Bishop Harman forceps.

## AIR GONIOTOMY

If goniotomies have not reduced the pressure sufficiently and gonioscopy shows that further repetition of goniotomy in the nasal portion of the angle is not feasible because of iris adhesions or scar formation, an attempt may be made to perform a goniotomy under air in the temporal portion of the angle. This area can be made visible by filling the chamber with air.[8,9] Since it is difficult consistently to insufflate the whole anterior chamber with air through a corneal puncture, an oblique scleral incision as for cyclodialysis is used and the sterile air injected by means of a curved gold cannula and small Luer syringe. The eye is then fixated with two Gifford forceps with lock and abducted. The temporal limbus disappears behind the canthus. The operator stands on the opposite side. The knife is passed across the bridge of the infant's nose and the cornea punctured 1 mm. axial to the nasal corneo-scleral border. Goniotomy under air or " air goniotomy " of the temporal portion of the angle is performed. Only a gross picture of the insertion of the root of the iris is discernible through air, due to the opacities of the cornea, to reflections and to absence of magnification. However, visibility may be sufficient when combined with familiarity of the angle to act as a guide to the blade of the knife.

*Blunt Dissection.* Blunt dissection of the angle with a spatula inserted through a prelaid corneal puncture has been tried in place of stripping or peeling of the angle with a goniotomy knife. In practice this has shown no advantage over the present technique with the knife; on the contrary it appears to encourage adhesion of the root of the iris and closure of the angle.

* The knife, surgical contact glass and hammer lamp can be obtained from A. H. Parsons Laboratories, 442 Post Street, San Francisco, 2, California. The knife will be obtainable also from E. Grieshaber, Schaffhausen, Switzerland. Recently specifications for its present form have been sent to V. Mueller and to Storz.

*Goniotomy Knife.* The shaft of the knife is conoid in order to prevent loss of aqueous. Its diameter increases progressively from the tip of the blade to the heel of the shaft. The blade is not too sharp as it is used to strip or peel and not to incise, the tip being sharp enough, however, to permit easy puncture of the cornea. Some resistance is felt during the stripping, which gives the operator a feeling of guidance and deliberate movement.

## SUMMARY

Congenital glaucoma in the past has resulted in a high percentage of blindness, due to lack of an adequate operation.

Goniotomy, performed at this writing on 76 eyes afflicted with infantile glaucoma, preserved useful vision in most cases. In 66 eyes pressure was normalized and vision maintained or restored over periods ranging from one to ten years. In ten the operation was unsuccessful. When combined with early diagnosis it provided excellent visual results.

A plea is made for early diagnosis and prompt, adequate operation by goniotomy.

The symptoms of increased intra-ocular pressure in congenital glaucoma may be present at birth, or their onset may be rapid or sudden during the first few months of infancy. In most cases symptoms consist of cloudy cornea, photophobia and other signs of irritation and congestion. Diagnosis should be made as soon as possible after onset of congestive symptoms and not deferred until enlargement of the eye is evident. In the rare cases of slow onset there are no congestive symptoms. Pressure should be measured with a tonometer under ether anaesthesia, which must be sufficient to assure complete relaxation at the moment of measurement.

The appearance of congestive symptoms is prone to lead to a faulty diagnosis of blepharitis, conjunctivitis or keratitis, causing loss of valuable time and bearing tragic consequences.

The initial cloudiness of the cornea is associated with roughening of the corneal epithelium. This disturbance of the cornea is the chief cause of the irritative symptoms and photophobia. If the corneal cloudiness is allowed to persist, it is superseded by permanent scarring with associated irregular astigmatism and ensuing amblyopia of greater or less degree.

Glaucomatous atrophy of the optic nerve was the exception in this series of infants and children. It occurred only in those few cases in which normalization of pressure was unduly delayed. In infants it is not nearly as urgent to protect the optic nerve-head from pressure as it is to relieve cloudiness of the cornea.

If soon after its inception increased intra-ocular pressure is normalized by goniotomy, transparency of the cornea is almost completely restored and maintained, and vision is afforded the opportunity to develop. When this is borne in mind, the urgency of prompt relief of increased pressure is evident.

The mode of action, advantages and disadvantages, indications and contra-indications of goniotomy are given.

The technique of goniotomy is described.

The author wishes to express his appreciation to his colleagues who have referred these patients, as well as to Childrens' Hospital, San Francisco, for its helpful co-operation,

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